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Osteomyelitis of the Jaws

Foreword by Robert E. Marx



Marc M. Baltensperger • Gerold K. H. Eyrich (Eds.)

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Foreword by Robert E. Marx
With 537 Figures and 47 Tables



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Aspects of the Human Face
(oil on canvas 200 × 120 cm)
Marc M. Baltensperger, 2000
mmbaltartproject.com

Dedication

This book is dedicated to my wife Chrisellee, my son Glen and Kevin. Without their continuous love, support and understanding, this book would not have been possible.

MARC M. BALTENSPERGER

*Everything should be made as simple as possible,
but not one bit simpler.*

ALBERT EINSTEIN (1879–1955)

Classification and re-classification of a subject over and over again with reference to other differentiating factors, makes one able to achieve a fresh approach each time.

VIMANASTHAANA IN CHARAKA SAMITHA 6:4
ANCIENT AYURVEDIC SUTRA, 7 B.C.

Medicine as a science is continuously changing. Research and clinical experience increase our knowledge, in particular regarding treatment and medical therapy. Where in this work a dosage or an application is mentioned, the reader may trust that the authors, editors, and publisher have gone to great lengths to ensure that this information corresponds exactly to **current knowledge at the time of publication**.

However, each user is required to read the instruction leaflet for the medication to check for himself or herself if the recommended dosage or the contraindications given therein differ from the information given in this book. This applies especially for medication that is rarely used or that has only recently come on the market and for those medications whose use has been restricted by Federal Health authorities.

MARC M. BALTENSPERGER
GEROLD K. H. EYRICH

Special Thanks

This textbook, in its present form, would not have been possible without the support and input of several people who have accompanied us on this journey. Some of them have directly contributed to this book as coauthors; others have given us valuable ideas and thoughts, which we have integrated in this book. Our special thanks go to these friends and colleagues.

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Foreword

Osteomyelitis of the jaws is a disease that has affected mankind since prehistory. In fact, the famous 1.6 million-year-old fossil find of "Turkana Boy" documents this very well. As a 12-year-old prehuman hominid (homo erectus) his nearly complete skeleton clearly showed an osteomyelitis arising from an odontogenic infection around one of his first molar teeth (Fig.1). Paleontologists even conjecture that it was the most likely cause of his premature death. Today, medical and dental specialists continue to treat osteomyelitis of various types with the recognition that osteomyelitis of the jaws differs significantly from osteomyelitis of the long bones and at other skeletal sites. These differences are due to a different group of pathogens, the presence of teeth, a different blood vessel density, an oral environment, a thin mucosa as opposed to skin, one jaw that is mobile and the other that is fixed, the more frequent presence of foreign bodies, and the commonality of head and neck radiotherapy. These differences are also reflected in the confusing array of terms used to describe the different forms of jaw osteomyelitis, e.g., chronic diffuse sclerosing osteomyelitis, Garré's osteo-



Fig. 1 Mandible of the "Turkana Boy". Picture courtesy of National Museums of Kenya, Palaeontology Department, Nairobi, Kenya

myelitis with Proliferative periostitis, periostitis ossificans, etc., as well as many entities that are not primarily infectious etiologies but develop a secondary osteomyelitis by virtue of exposed bone in the oral cavity such as osteoradionecrosis, osteopetrosis, and bisphosphonate-induced osteonecrosis.

In this book, M. Baltensperger and G. Eyrich begin with a straightforward classification and terminology system that is consistent with the scientific evidence of the different clinical forms of jaw osteomyelitis. They further coordinate the initiating factors, host local and systemic factors, and pathogenesis to the clinical presentation. In a logical manner, useful to the student, resident, and senior clinicians alike, a differential diagnostic methodology is offered, inclusive of clear descriptions of what the present imaging technology can and cannot offer. This is followed by separate chapters on the different microscopic pathologies seen with each type of osteomyelitis and the microbiology of the known pathogens. The next three chapters are focused on treatment. They logically begin with the principles of treatments including the selection of the most appropriate surgical procedure and its follow-up by the selection of the appropriate antibiotic, as well as its correct dosing and the role of adjunctive hyperbaric oxygen in selected cases. The next chapter openly discussed the uniqueness of osteomyelitis involving the temporomandibular joint and its treatment, a disease not often discussed in other texts. The final chapter underscores the practical value of this book. In an innovative manner the authors present 20 case reports of actual cases and how they were diagnosed and further managed. These cases encompass nearly the full spectrum of osteomyelitis of the jaws and support the application of the principles and techniques reviewed in the preceding chapter.

The reader should appreciate the flow of this book, from the history of osteomyelitis to its classification, diagnosis, pathology, imaging, and treatment. The reader should also appreciate that a complex disease, such as osteomyelitis of the jaws with numerous variations, can be simplified in approach while still retaining the comprehensiveness of its diagnosis and treatment. The student can use this book as a comprehensive textbook or on a chapter-by-chapter basis. The experienced clinician can use the book for general review or as a case review as he or she may be confronted with their own challenging case. Both groups will find the case reports to be the realistic element that brings everything together.

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Preface

Writing and editing a book naturally gives rise to questions regarding the deeper motivations for undertaking such work. Some topics seem to accompany one during one's daily work life: They even seem to be sitting in the waiting area when you enter the office in the morning. When this happens, we start to become more obsessed with the attendant difficulties of the discipline. Finding oneself wrong, or perhaps ill-equipped with the tools and knowledge available, can often deepen the quest for solutions. For us, osteomyelitis of the jaws has become a complex matter that has not been resolved by current research, but we have certainly made significant progress.

Everyone can visualize the faces and anxiety of the parents of a 12-year-old boy being confronted with the possible diagnosis of a malignant disease. In one case, soon after we had assuaged the initial fear of a life-threatening disease away, we found ourselves confronted with primary chronic osteomyelitis. Fear was clearly seen in the parents' faces when we explained that we did not really have a reliable treatment option, and that neither did we know the cause or prognosis of the disease. Consequently, the disorder has become a "face," insofar as not only the disorder but also the patient "accompanies" you as you try to determine the treatment. This uncertainty is even more astonishing since we encounter osteomyelitis frequently in our daily practice. Many people may assume that osteomyelitis has been thoroughly researched and resolved, especially inexperienced residents. When looking for signposts, guidelines, or definitions, however, the road becomes ambiguous. For example, several terms have been used for the same conditions, and there are numerous classification systems, descriptions, and recommendations. The inevitable question is: Which road should one take, and which opinions should one follow?

Once a path has been chosen, one must constantly verify and justify courses of action and treatment options. This will help us to understand the treatment process and keep focused on the goal. Without engaging in this self-inquiry, however, one cannot make much progress.

Although we use a classification system in this book which is very familiar to us, we have tried to render it understandable to everyone. We have combined our knowledge and experience so that readers will not be prone to the pitfalls which have marked our journey. In retrospect, there have always been signposts along the road. Some of the questions have been solved and others have increased in complexity. Up to now, it appears that no comprehensive book on osteomyelitis of the jaws has been attempted. It is our deepest hope that this book will be a significant contribution that will help guide the reader in choosing the best roads and vehicles on this journey.

Marc Baltensperger and Gerold Eyrich

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1 Introduction

Marc Baltensperger and Gerold Eyrich

Osteomyelitis of the jaws is still a very unique disease of the facial skeleton that represents a great challenge for the physician as well as the patient being treated, despite all recent advances in diagnosis and evolved treatment modalities. In the past decades the clinical appearance of osteomyelitis cases has changed dramatically. Not only has the average number of cases seen in a maxillofacial unit decreased, but also the clinical picture of the disease itself has changed significantly. Osteomyelitis of the jaws used to be an infectious disease with an often complicated course, involving multiple surgical interventions and sometimes leading to facial disfigurement as a result of loss of affected bone and teeth and the accompanying scarring. The outcome was usually all but certain; hence, prolonged treatment and frequent relapses have been associated with this disease in the past.

Since the second half of the twentieth century, however, there has been a dramatic reduction in the incidence of osteomyelitis cases involving the jaws and other bones of the skeleton (Hudson 1993). One major probable factor leading to this development is the introduction of antibiotics into the therapeutic armamentarium; however, other factors have also contributed, such as improved nutrition and better availability of medical and dental care, especially including advances in preventive dentistry and oral hygiene. Earlier diagnosis due to more sophisticated diagnostic imaging modalities has additionally improved the morbidity associated with this disease (Hudson 1993; Topazian 2002).

While the abovementioned factors are accounted for in most Western countries, this is still not the case for all of them. There are numerous countries with great deficiencies in their medical and social systems, unable to give adequate medical treatment to all people in need. In such an environment severe courses of osteomyelitis involving the jaws are still frequently observed. The statistics of medical institutions which deal with osteomyelitis of the jaws in these regions resemble those seen in Western maxillofacial units several decades ago (Adekeye 1976; Adekeye and Cornah 1985; Taher 1993).

Despite all the benefits associated with the advances in medicine and dentistry, the development of microorganisms resistant to commonly used antibiotics, the increased number of patients treated with steroids and other immunocompromising drugs, and the rising incidence of AIDS, diabetes, and other medically compromising conditions have led to new problems in the treatment of osteomyelitis of the jaws, leading again to an increase of cases refractory to standard treatments. Radiation therapy leading to osteoradionecrosis has also been a condition which, if super-infected, has contributed to a large number of complicated osteomyelitis cases in the past decades. Due to more localized and fractioned application of radiation, and the consequent prophylactic dental treatment of these patients, these sometimes jaw-mutilating courses of the disease have become less frequent.

Recently, an increasing number of patients treated with bisphosphonates have been noted to develop osteonecrosis of the jawbone. This condition, also known as osteochemonecrosis, presents a condition which favors the development of osteomyelitis. The widespread use of bisphosphonates foreshadows that the number of cases with this condition will even rise in the future; however, presently in most maxillofacial units the number of osteomyelitis cases of the jaws seen by the single physician has decreased over the past decades. This may lead to a lack of experience in managing this disease with its unique manifestations in the jaw.

The numerous reports in the literature on osteomyelitis of the jaws reflects the importance of this disease, especially in the maxillofacial specialty. Several authors have undertaken the task of describing the disease and classifying its various types. This rich diversity of literature has also led to some confusion and many inconsistencies. The various classification systems advocated over the years have resulted in a great variety in terminology and have made comparative studies on an evidence basis extremely difficult, if not impossible. Although classification systems are described in several textbooks and journals, only few authors have demonstrated a classification system on a substantial number of cases and, hence, one of practical use for the treating physician.

The foundation of this textbook lies in a large study which retrospectively analyzed the osteomyelitis cases treated in the past three decades at the Department of Cranio-Maxillofacial Surgery at the University Hospital in Zurich. In this study conducted by my coeditor, Gerold Eyrich, and myself, 290 well-documented cases of osteomyelitis of the jaws were included (Baltensperger 2003). It represents, to our knowledge, the largest examined patient group with this disease in the literature to date. The main purpose of this study was to classify these cases based on the classification system for osteomyelitis used in this unit. Throughout the study, meticulous work-up of all the patient data revealed the benefits as well as the drawbacks of the used classification system. In conclusion, some modifications compared with the commonly used classification systems have been made where we thought them to be beneficial. The definitions of certain categories were refined. Some terms have been abandoned. In the case of primary chronic osteomyelitis a new subclassification was proposed which seemed to be justified based on our patient data and other recent publications.

The advocated classification system for osteomyelitis of the jaws is the core of this book. It is referred to as the Zurich classification for osteomyelitis of the jaws. Most of the coauthors contributing to this book have already been involved in the above-mentioned study and/or have participated in other recent publications on this topic where the same classification was used; therefore, the proposed classification system advocated in this book is consistently applied in each chapter.

It was our purpose to cover every aspect of this disease from classification to diagnosis and treatment. This book consists of 11 additional chapters which are all intended to stand on their own, with separate tables of contents and references and a summary at the beginning. This allows the reader who is particularly interested in one aspect of the disease a quick overview of the topic; however, certain redundancies from chapter to chapter are deliberately taken in account.

Because of the predominant role of diagnostic imaging in the diagnosis and classification of osteomyelitis (see Table 2.7 in Chap. 2), an entire chapter is dedicated to this special topic, highlighting standard conventional radiographic imaging modalities as well as the latest technologies in use.

Other chapters focus on pathology and microbiology, which are necessary topics in understanding the nature of this complex disease. In the past, osteomyelitis of the jaws, in analogy to long bone infection, was believed to be primarily caused by *Staphylococcus aureus*, *Staphylococcus epidermidis*, or hemolytic *Streptococci*. The discovery of several anaerobic bacteria involved in jawbone infection has broadened our knowledge in understanding the microbiology of this disease and is outlined in detail.

Pathology has always been regarded as valuable in the diagnostic process of osteomyelitis, especially in distinguishing it from other diseases of the bone. The specific aspects of infections of the jawbone are discussed in detail.

The chapter which deals with therapy of osteomyelitis of the jaws is divided into surgical therapy, antibiotic therapy, and hyperbaric oxygen therapy, which are considered the major columns of osteomyelitis treatment to date.

Because of its unique location and rare incidence, osteomyelitis of the mandible affecting the temporomandibular joint is very demanding to treat and always represents a great challenge. We therefore considered a separate chapter for this issue to be justified.

The final chapter is designed as an atlas. Typical case reports as well as cases with a complex course of each osteomyelitis category are described and illustrated, rounding out the scope of this book.

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2 Osteomyelitis of the Jaws: Definition and Classification

Marc Baltensperger and Gerold Eyrich

Contents

2.1 Summary

Osteomyelitis of the jaws is still a fairly common disease in maxillofacial clinics and offices, despite the introduction of antibiotics and the improvement of dental and medical care. The literature on this disease is extensive. Different terminologies and classification systems are used based on a variety of features such as clinical course, pathological–anatomical or radiological features, etiology, and pathogenesis. A mixture of these classification systems has occurred throughout the literature, leading to confusion and thereby hindering comparative studies. An overview of the most commonly used terms and classification systems in osteomyelitis of the jaws is given at the beginning of this chapter.

The Zurich classification system, as advocated in this textbook, is primarily based on the clinical course and appearance of the disease as well as on imaging studies. Subclassification is based on etiology and pathogenesis of the disease. Mainly three different types of osteomyelitis are distinguished: acute and secondary chronic osteomyelitis and primary chronic osteomyelitis. Acute and secondary chronic osteomyelitis are basically the same disease separated by the arbitrary time limit of 1 month after onset of the disease. They usually represent a true bacterial infection of the jawbone. Suppuration, fistula formation, and sequestration are characteristic features of this disease entity. Depending on the intensity of the infection and the host bone response, the clinical presentation and course may vary significantly. Acute and secondary chronic osteomyelitis of the jaws is caused mostly by a bacterial focus (odontogenic disease, pulpal and periodontal infection, extraction wounds, foreign bodies, and infected fractures).

Primary chronic osteomyelitis of the jaw is a rare, nonsuppurative, chronic inflammation of an unknown cause. Based on differences in age at presentation,

clinical appearance and course, as well as radiology and histology, the disease may be subclassified into early- and adult-onset primary chronic osteomyelitis. Cases with purely mandibular involvement are further distinguished from cases associated with extragnathic dermatoskeletal involvement such as in SAPHO syndrome or chronic recurrent multifocal osteomyelitis (CRMO).

2.2 Definition

The word "osteomyelitis" originates from the ancient Greek words osteon (bone) and muelinos (marrow) and means infection of medullary portion of the bone. Common medical literature extends the definition to an inflammation process of the entire bone including the cortex and the periosteum, recognizing that the pathological process is rarely confined to the endosteum. It usually encompasses the cortical bone and periosteum as well. It can therefore be considered as an inflammatory condition of the bone, beginning in the medullar cavity and havarian systems and extending to involve the periosteum of the affected area. The infection becomes established in calcified portion of the bone when pus and edema in the medullary cavity and beneath the periosteum compromises or obstructs the local blood supply. Following ischemia, the infected bone becomes necrotic and leads to sequester formation, which is considered a classical sign of osteomyelitis (Topazian 1994, 2002).

Although other etiological factors, such as traumatic injuries, radiation, and certain chemical substances, among others, may also produce inflammation of the medullar space, the term "osteomyelitis" is mostly used in the medical literature to describe a true infection of the bone induced by pyogenic microorganisms (Marx 1991).

2.3 History

The prevalence, clinical course, and management of osteomyelitis of the jawbones have changed profoundly over the past 50 years. This is due to mainly one factor: the introduction of antibiotic therapy, specifically penicillin. The integration of antibiotics into the therapeutic armamentarium has led to a complete renaissance in the treatment of most infectious diseases, including osteomyelitis (Hudson 1993). Further factors, such as sophistication in medical and dental science as well as the widespread availability for adequate treatment, have additionally led to improvement in the management of this disease. Modern diagnostic imaging allows much earlier treatment of bone infections at a more localized stage.

In the preantibiotic era, the classical presentation of jawbone osteomyelitis was an acute onset, usually followed by a later transition to a secondary chronic process (Wassmund 1935; Axhausen 1934). Massive clinical symptoms with widespread bone necroses, neoosteogenesis, large sequester formation, and intra- and extraoral fistula formation were common presentations, sometimes leading to significant facial disfigurement (Fig. 2.1).

After the introduction of antibiotics, acute phases were often concealed by these antimicrobial drugs without fully eliminating the infection. Subacute or chronic





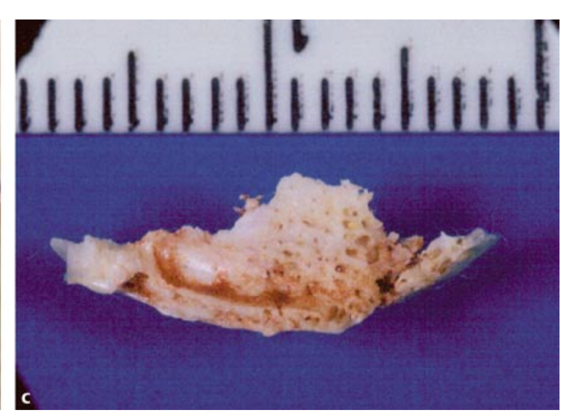


Fig. 2.1a–c Elder case of advanced secondary chronic osteomyelitis of the left mandible. The massive affection of the left mandible demonstrates extraoral fistula and scar formation (**a**). Intraoral view of the same patient with large exposure of infected bone and sequestra (**b**). Large sequester collected from surgery (**c**) (Courtesy of N. Hardt)

forms of osteomyelitis have therefore become more prominent, lacking an actual acute phase (Becker 1973; Bünger 1984).

2.4 Overview of Currently Used Classification Systems and Terminology

One of the first widely accepted staging systems for osteomyelitis in long bones was first described by Waldvogel and Medoff (1970) and Waldvogel et al. (1970a,b). The authors distinguished three categories of osteomyelitis: osteomyelitis from hematogenous spread; from a contagious focus; and due to vascular insufficiency. The classification is primarily based on etiology and pathogeneses of infection and does not readily lend itself to guiding therapeutic strategies such as surgery and antibiotic therapy. A more comprehensive classification proposed by Cieny et al. (1985) and Mader and Calhoun (2000) is based upon the anatomy of the bone infection and the physiology of the host. It divides the disease into four stages combining four anatomical disease types and three physiological host categories resulting in the description of 12 discrete clinical stages of osteomyelitis. Such a classification system, although it may be important in dealing with numerous sites of the skeletal system and allowing stratification of infection and the development of comprehensive treatment guidelines for each stage, is unnecessarily complex and impractical when dealing with infections of the jawbones.

Because of its unique feature bearing teeth and hence connecting to the oral cavity with the periodontal membrane, osteomyelitis of the jaws differs in several

Table 2.1 Classification systems described in the literature for osteomyelitis of the jaws

Reference	Classification	Classification criteria
Hudson JW Osteomyelitis of the jaws: a 50-year perspective. *J Oral Maxillofac Surg 1993 Dec; 51(12):1294-301*	I. Acute forms of osteomyelitis (suppurative or nonsuppurative) A. Contagious focus 1. Trauma 2. Surgery 3. Odontogenic Infection B. Progressive 1. Burns 2. Sinusitis 3. Vascular insufficiency C. Hematogenous(metastatic) 1. Developing skeleton (children) II. Chronic forms of osteomyelitis A. Recurrent multifocal 1. Developing skeleton (children) 2. Escalated osteogenic (activity < age 25 years) B. Garrè's 1. Unique proliferative subperiosteal reaction 2. Developing skeleton (children and young adults) C. Suppurative or nonsuppurative 1. Inadequately treated forms 2. Systemically compromised forms 3. Refractory forms (chronic recurrent multifocal osteomyelitis CROM) D. Diffuse sclerosing 1. Fastidious microorganisms 2. Compromised host/pathogen interface	Classification based on clinical picture and radiology. The two major groups (acute and chronic osteomyelitis) are differentiated by the clinical course of the disease after onset, relative to surgical and antimicrobial therapy. The arbitrary time limit of 1 month is used to differentiate acute from chronic osteomyelitis (Marx 1991; Mercuri1991; Koorbusch1992).

Table 2.2 Classification systems described in the literature for osteomyelitis of the jaws

Reference	Classification	Classification criteria
Hudson JW Osteomyelitis of the jaws: a 50-year perspective. *J Oral Maxillofac Surg 1993 Dec;51(12):1294-301*	I. Hematogenous osteomyelitis II. Osteomyelitis secondary to a contiguous focus of infection III. Osteomyelitis associated with or without peripheral vascular disease	Classification based on pathogenesis. From Vibhagool 1993
Hudson JW Osteomyelitis of the jaws: a 50-year perspective. *J Oral Maxillofac Surg 1993 Dec;51(12):1294-301*	I. Anatomic Types Stage I: medullar osteomyelitis – involved medullar bone without cortical involvement; usually hematogenous Stage II: superficial osteomyelitis – less than 2 cm bony defect without cancellous bone Stage III: localized osteomyelitis – less than 2 cm bony defect on radiograph, defect does not appear to involve both cortices Stage IV: diffuse osteomyelitis – defect greater than 2 cm. Pathologic fracture, infection, nonunion II. Physiological class A host: normal host B host: systemic compromised host, local compromised host C host: treatment worse than disease	Dual classification based on pathological anatomy and pathophysiology From Vibhagool 1993 and Cierny 1985
Mittermayer CH Oralpathologie. *Schattauer, Stuttgart-New York 1976*	I. Acute suppurative osteomyelitis (rarefactional osteomyelitis) II. Chronic suppurative osteomyelitis (sclerosing osteomyelitis) III. Chronic focal sclerosing osteomyelitis (pseudo-paget, condensing osteomyelitis) IV. Chronic diffuse sclerosing osteomyelitis V. Chronic osteomyelitis with proliferative periostitis (Garrè's chronic nonsuppurative sclerosing osteitis, ossifying periostitis) VI. Specific osteomyelitis 1. Tuberculous osteomyelitis 2. Syphilitic osteomyelitis 3. Actinomycotic osteomyelitis	Classification based on clinical picture, radiology, pathology, and etiology

important aspects from osteomyelitis of long bones. The specific local immunological and microbiological aspects determine a major factor in the etiology and pathogenesis of this disease, and hence also have a direct impact on its treatment; therefore, to extrapolate from long bone infections to disease of the jaws is only possible with limitations. This is reflected by the long-standing recognition of osteomyelitis of jawbones as a clinical entity, which differs in many important aspects from the one found in long bones; hence, a wide variety of classifications, specifically for the jawbones, have been established by several authors in the medical literature. Classifications proposed are based on different aspects such as clinical course, pathological–anatomical

Table 2.3 Classification systems described in the literature for osteomyelitis of the jaws

Reference	Classification	Classification criteria
Hjorting-Hansen E Decortication in treatment of osteomyelitis of the mandible. *Oral Surg Oral Med Oral Pathol 1970 May;29(5):641-55*	I. Acute/subacute osteomyelitis II. Secondary chronic osteomyelitis III. Primary chronic osteomyelitis	Classification based on clinical picture and radiology
Marx RE Chronic Osteomyelitis of the Jaws *Oral and Maxillofacial Surgery Clinics of North America, Vol 3, No 2, May 91, 367-81* Mercuri LG Acute Osteomyelitis of the Jaws *Oral and Maxillofacial Surgery Clinics of North America, Vol 3, No 2, May 91, 355-65*	I. Acute osteomyelitis 1. Associated with Hematogenous spread* 2. Associated with intrinsic bone pathology or peripheral vascular disease* 3. Associated with odontogenic and nonodontogenic local processes* II. Chronic osteomyelitis 1. Chronic recurrent multifocal osteomyelitis of children 2. Garrè's osteomyelitis 3. Chronic suppurative osteomyelitis – Foreign body related – Systemic disease related – Related to persistent or resistant organisms 4. True chronic diffuse sclerosing osteomyelitis	Classification based on clinical picture and radiology, etiology, and pathophysiology Classification of acute osteomyelitis by Mercuri, classification of chronic osteomyelitis by Marx. The arbitrary time limit of one month is used to differ acute from chronic osteomyelitis * From Waldvogel and Medoff 1970
Panders AK, Hadders HN Chronic sclerosing inflammations of the jaw. Osteomyelitis sicca (Garre), chronic sclerosing osteomyelitis with fine-meshed trabecular structure, and very dense sclerosing osteomyelitis. *Oral Surg Oral Med Oral Pathol 1970 Sep;30(3):396-412*	I. Primarily chronic jaw inflammation 1. Osteomyelitis sicca (synonymous osteomyelitis of Garrè, chronic sclerosing nonsuppurative osteomyelitis of Garrè, periostitis ossificans) 2. Chronic sclerosing osteomyelitis with fine-meshed trabecular structure 3. Local and more extensive very dense sclerosing osteomyelitis II. Secondary chronic jaw inflammation III. Chronic specific jaw inflammations – Tuberculosis – Syphilis – Lepra – Actinomycosis	Classification based on clinical picture and radiology Classification of chronic osteomyelitis forms only

and/or radiological features, etiology, and pathogenesis. A mixture of these classification systems has been used in many instances, leading to confusion and thereby hindering comparative studies and obscuring classification criteria. An overview of the most commonly cited classifications of jawbone osteomyelitis are listed in Tables 2.1–2.4.

Table 2.4 Classification systems described in the literature for osteomyelitis of the jaws

Reference	Classification	Classification criteria
Schelhorn P, Zenk W [*Clinics and therapy of the osteomyelitis of the lower jaw*]. *Stomatol DDR 1989 Oct;39(10):672-6*	I. Acute osteomyelitis II. Secondary chronic osteomyelitis III. Primary chronic osteomyelitis IV. Special forms – Osteomyelitis sicca (pseudo-paget Axhausen) – Chronic sclerosing osteomyelitis Garrè	Classification based on clinical picture
Topazian RG *Osteomyelitis of the Jaws. In Topizan RG, Goldberg MH (eds): Oral and Maxillofacial Infections.* *Philadelphia, WB Saunders 1994, Chapter 7, pp 251-88*	I. Suppurative osteomyelitis 1. Acute suppurative osteomyelitis 2. Chronic suppurative osteomyelitis – Primary chronic suppurative osteomyelitis – Secondary chronic suppurative osteomyelitis 3. Infantile osteomyelitis II. Nonsuppurative osteomyelitis 1. Chronic sclerosing osteomyelitis – Focal sclerosing osteomyelitis – Diffuse sclerosing osteomyelitis 2. Garrè's sclerosing osteomyelitis 3. Actinomycotic osteomyelitis 4. Radiation osteomyelitis and necrosis	Classification based on clinical picture, radiology, and etiology (specific forms such as syphilitic, tuberculous, brucellar, viral, chemical, *Escherichia coli* and *Salmonella* osteomyelitis not integrated in classification)
Bernier S, Clermont S, Maranda G, Turcotte JY *Osteomyelitis of the jaws.* *J Can Dent Assoc 1995 May;61(5):441-2, 445-8*	I. Suppurative osteomyelitis 1. Acute suppurative osteomyelitis 2. Chronic suppurative osteomyelitis II. Nonsuppurative osteomyelitis 1. Chronic focal sclerosing osteomyelitis 2. Chronic diffuse sclerosing osteomyelitis 3. Garrè's chronic sclerosing osteomyelitis (proliferative osteomyelitis) III. Osteoradionecrosis	Classification based on clinical picture and radiology
Wassmund M Lehrbuch der praktischen Chirurgie des Mundes und der Kiefer. *Meusser, Leipzig 1935*	I. Exudative osteitis II. Resorptive osteitis III. Productive osteitis IV. Acute necrotizing osteitis (osteomyelitis) V. Chronic osteomyelitis 1. Chronic course of an acute osteomyelitis 2. Occult osteomyelitis 3. Chronic necrotizing osteomyelitis with hypertrophy 4. Chronic exudative osteomyelitis 5. Productive osteomyelitis	Classification based on clinical picture and radiology (note that classification was developed before introduction of antibiotic therapy)

2.5 Currently Used Terms in Classification of Osteomyelitis of the Jaws

2.5.1 Acute/Subacute Osteomyelitis

Although acute forms of osteomyelitis are seen only rarely these days, most authors in common medical literature still describe this form as an entity of its own. Mercuri (1991) and Marx (1991) arbitrarily defined the time element as being 1 month after onset of symptoms. Endurance past this arbitrary set time limit is then considered as chronic osteomyelitis reflecting the inability of host defense mechanisms to eradicate the responsible pathogen. Many authors have agreed on this classification and have used the term likewise in their publications (Koorbusch et al. 1992; Hudson 1993; Schuknecht et al. 1997; Schuknecht and Valavanis 2003; Eyrich et al. 1999; Baltensperger et al. 2004).

The term "subacute osteomyelitis" is not clearly defined in the literature. Many authors use the term interchangeably with acute osteomyelitis, and some use it to describe cases of chronic osteomyelitis with more prominent (subacute) symptoms. In some instances, subacute osteomyelitis is referred to as a transitional stage within the time frame of acute osteomyelitis and corresponds to the third and fourth week after onset of symptoms (Schuknecht et al. 1997; Schuknecht and Valavanis 2003).

2.5.2 Chronic Osteomyelitis

The classification of chronic osteomyelitis is incoherent and confusing. Different disease processes have been described by this one term in some instances, whereas several terms have been designated for lesions that represent the same entity in other instances (Groot et al. 1996; Eyrich et al. 1999).

Many authors agree that chronic osteomyelitis involving the jawbone may be divided in two major categories: suppurative and nonsuppurative forms (Mittermayer 1976; Hudson 1993; Topazian 1994, 2002; Bernier et al. 1995).

2.5.3 Chronic Suppurative Osteomyelitis: Secondary Chronic Osteomyelitis

Chronic suppurative osteomyelitis is an often preferred term in Anglo-American texts (Marx 1991; Bernier et al. 1995; Topazian 1994, 2002) and can mostly be used interchangeably with the term "secondary chronic osteomyelitis," which is predominantly used in literature from continental Europe (Hjorting-Hansen 1970; Panders and Hadders 1970; Schelhorn and Zenk 1989). It is by far the most common osteomyelitis type, which is usually caused by bacterial invasion from a contagious focus. Most frequent sources are odontogenic foci, periodontal diseases and pulpal infections, extraction wounds, and infected fractures. Pus, fistula, and sequestration are typical clinical findings of this disease. Clinically and radiographically, a broad spectrum ranging from an aggressive osteolytic putrefactive phase to a dry osteosclerotic phase may be observed (Eyrich et al. 1999).

2.5.4 Chronic Non-suppurative Osteomyelitis

The term "nonsuppurative osteomyelitis" describes a more heterogenic group of chronic osteomyelitis forms, which lacks the formation of pus and fistula. Topazian (1994, 2002) includes chronic sclerosing types of osteomyelitis, proliferative periostitis, as well as actinomycotic and radiation-induced forms to this group, whereas Bernier et al. (1995) advocate a more restrictive use of this term. Hudson (1993) uses the term to describe a condition of prolonged refractory osteomyelitis due to inadequate treatment, a compromised host, or increased virulence and antibiotic resistance of the involved microorganisms. This classification therefore also incorporates those cases in which a suppurative form of osteomyelitis can present as a nonsuppurative form in an advanced stage.

2.5.5 Diffuse Sclerosing Osteomyelitis, Primary Chronic Osteomyelitis, Florid Osseous Dysplasia, Juvenile Chronic Osteomyelitis

One of the most confusing terms among the currently used osteomyelitis nomenclature is "diffuse sclerosing osteomyelitis" (DSO). This term has apparently led to great confusion in the medical literature. A variety of denominations were used to describe this disease. One of the first descriptions was by Thoma in 1944, who used the term "ossifying osteomyelitis" and considered that a disease which was caused by a subpyogenic infection that could be found in tertiary syphilis. Sclerosing osteomyelitis was later described and divided into a focal

and diffuse types (Shafer 1957; Shafer et al. 1974; Pindborg and Hjorting-Hansen 1974; Mittermayer 1976; Topazian 1994, 2002). The focal type, also known as periapical osteitis/osteomyelitis or condensing osteitis, is a rather common condition with a pathognomonic, well-circumscribed radioopaque mass of sclerotic bone surrounding the apex of the root. Since the infection in these cases is limited to the apex of the root with the absence of deep bone invasion, sufficient endodontic treatment with or without apex surgery or extraction of the affected tooth usually leads to regression of these lesions or residual sclerosis may remain as a bone scar.

True diffuse sclerosing osteomyelitis, however, is a rare disease of unknown etiology that can cause major diagnostic and therapeutic problems (Jacobson 1984). The absence of pus, fistula, and sequestration are characteristic. The disease shows an insidious onset, lacking an acute state. It is therefore considered to be primary chronic and has been named primary chronic osteomyelitis by several authors, predominantly in the German and continental European medical and dental literature (Hjorting-Hansen 1970; Panders and Hadders 1970; Schelhorn and Zenk 1989; Eyrich at al 1999). Periods of onset usually last from a few days up to several weeks and may demonstrate a cyclic course with symptom-free intervals. Pain, swelling, and limitation of mouth opening, as well as occasional lymphadenopathy, dominate the clinical picture.

The term DSO is primarily descriptive of the radiological appearance of the pathological bone reaction; however, although the term is usually used synonymously with primary chronic osteomyelitis, it represents a description of a strictly radiological appearance that can be caused by several similar processes. These processes include primary and secondary chronic osteomyelitis, chronic tendoperiostitis, and ossifying periostitis or Garrè's osteomyelitis (Hjorting-Hansen 1970; Ellis et al. 1977; Eisenbund et al. 1981; Bünger 1984; Van Merkestyn et al. 1990; Groot et al. 1992b, 1996; Eyrich et al. 1999). This fact has most likely contributed to this diversity in nomenclature, as the terms are often used interchangeably.

A further pathological disease entity has been confused with diffuse sclerosing osteomyelitis, since it may mimic DSO radiographically by presenting sclerosing opaque and dense masses: florid osseous dysplasia (FOD). These masses are, however, confined to the alveolar process of either or both jaws in cases of FOD. Florid osseous dysplasia is mostly observed in black women and in many cases lacks clinical symptoms. Patients suffering from this disease, similar to true DSO, may in some instances also experience cyclic episodes of unilateral pain and mild swelling. This is usually the case when superinfection occurs (Schneider et al. 1990; Groot et al. 1996)

As with all pathologies of the bone which compromise local blood flow and host resistance, FOD makes the jaw more susceptible to secondary infection. In these instances pus and fistula formation may occur as well as sequestration (Carlson 1994). Many cases like these in the literature have, in retrospect, been incorrectly labeled as diffuse sclerosing osteomyelitis where these symptoms are by definition always absent. The FOD should therefore be considered more a bone pathology facilitating osteomyelitis once infection of the bone has been established and not equated with the infection itself.

As mentioned above, the exact etiology of true DSO remains unknown. A common theory is a low-grade infection of some kind; however, most biopsy specimens taken from the enoral and extraoral approach have failed to be conclusive, showing either no growth in cultures or growth only from suspected contaminants (Jacobson et al. 1982; Jacobson 1984; Van Merkesteyn et al. 1988). A study by Marx et al. (1994) demonstrated a high frequency of *Actinomyces*, *E. corrodens* species, *Arachnia* and *Bacteroides* spp. in cortical and medullar samples from patients with DSO. This study, like many others, still demonstrated insufficiencies regarding the protocol for collecting bone specimens and therefore was inconclusive. Moreover, a variety of antibiotics used over a long period consistently failed to fully eradicate the disease or arrest the symptoms (Jacobson 1984; Van Merkesteyn et al. 1988, 1990). Van Merkesteyn et al. (1990) and Groot et al. (1992a) have advocated other etiologies such as aberrant jaw positioning and parafunction; however, their theory lacks an explanation for those cases of true DSO in edentulous patients.

In our recent publications (Eyrich et al. 1999, 2003; Baltesperger et al. 2004) we used the term "juvenile chronic osteomyelitis," which resembles the clinical and radiological picture of Garrè's osteomyelitis as used by various authors. Heggie et al. (2000, 2003) made a similar observation when analyzing his young osteomyelitis patients and used the term "juvenile mandibular chronic osteomyelitis." This disease usually peaks at puberty and is characterized mostly by voluminous expansion of the mandibular body, periosteal apposition of bone ("periostitis ossificans"), and a mixed sclerotic-lytic appearance of the cancellous bone. The clinical

picture resembles primary chronic osteomyelitis, sharing the lack of pus formation, fistulae, or sequestration. Juvenile chronic osteomyelitis is therefore considered to be an early-onset form of primary chronic osteomyelitis. A further and more detailed description of this disease entity is described later in this chapter.

2.5.6 SAPHO Syndrome, Chronic Recurrent Multifocal Osteomyelitis (CRMO)

In 1986 Chamot et al. described a syndrome associated with synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO syndrome). Soon, several case reports and studies were published, concluding a possible relationship between SAPHO syndrome and DSO of the mandible (Brandt et al. 1995; Kahn et al. 1994; Garcia-Mann et al. 1996; Suei et al. 1996; Schilling et al. 1999; Eyrich et al. 1999; Roldan et al. 2001; Fleuridas et al. 2002). Kahn et al. (1994) presented a small series of seven patients with DSO of the mandible out of 85 cases of SAPHO syndrome. Eyrich et al. (1999) presented a series of nine patients with DSO, eight of which also represented a SAPHO syndrome, supporting the hypothesis of a possible association of the two.

Chronic recurrent multifocal osteomyelitis (CRMO) is characterized by periods of exacerbations and remissions over many years. This rare disease is noted in adults as in children, although it is predominant in the latter group. In several articles published in the past few years, a possible nosological relationship between diffuse sclerosing osteomyelitis and chronic recurrent multifocal osteomyelitis has been described (Reuland et al. 1992; Stewart et al. 1994; Suei et al. 1994, 1995; Flygare et al. 1997; Zebedin et al. 1998; Schilling 1998; Schilling et al. 1999). In correlation with advanced age, there seems to be an increased association with palmoplantar pustulosis, a part of the SAPHO syndrome (Shilling et al. 2000). Because of its possible relationship with other dermatoskeletal associated diseases, CRMO has been integrated in the nosological heterogeneous SAPHO syndrome by several authors (Chamot et al. 1994; Schilling and Kessler 1998; Schilling et al. 2000).

2.5.7 Periostitis Ossificans, Garrès Osteomyelitis

Strictly periostitis ossificans or ossifying periostitis is, like diffuse sclerosing osteomyelitis, a descriptive term for a condition that may be caused by several similar entities. It is merely a periosteal inflammatory reaction to many nonspecific stimuli, leading to the formation of an immature type of new bone outside the normal cortical layer.

Probably the most confusing and misinterpreted term regarding osteomyelitis is “Garrè’s osteomyelitis.” While most medical pathologists discard the term, it has still enjoyed great acceptance in the medical and dental literature, where occurrence in the jaws has been termed unequivocally (Eversole et al. 1979). Many terms have been used synonymously in the literature and attributed to Garrè, such as periostitis ossificans, chronic nonsuppurative osteomyelitis of Garrè, Garrè’s proliferative periostitis, chronic sclerosing inflammation of the jaw, chronic osteomyelitis with proliferative periostitis, and many more. Table 2.5 gives an overview of the use of the term “Garrè’s osteomyelitis” in the medical and dental literature; however, in his historical article in 1893, Carl Garrè did not actually describe a singular, specific type of osteomyelitis. Moreover he described special forms and complications of a single disease: acute infective osteomyelitis. He used 72 illustrative cases (98 sites) to discuss ten specific manifestations and complications of acute osteomyelitis. This is a direct contradiction to those authors who assume that he described a new form of chronic osteomyelitis (Wood et al. 1988).

2.5.8 Other Commonly Used Terms

2.5.8.1 Alveolar Osteitis (Dry Socket)

The clinical term “dry socket” or alveolar osteitis may also be regarded as a localized form of infection. Various authors have used this term differently. Hjorting-Hansen (1960) describes three principle forms of dry socket: alveolitis simplex; alveolitis granulomatosa; and an alveolitis sicca. Amler (1973) differentiates among alveolar osteitis, suppurative osteitis, and fibrous osteitis. The author concludes that the three types of osteitis correspond to disturbances during the natural healing process of an extraction alveolus. Meyer (1971) took great effort in demonstrating the histopathological changes in alveolar osteitis. He classifies this condition according to the degree of local invasion of the surrounding bone and uses the terms “osteitis circumscripta superficialis”, “media” and “profunda”. The term latter may be seen as a localized form of osteomyelitis; however, the

Table 2.5 Use of the term Garrè's osteomyelitis in medical and dental literature

Reference	Term used	Type of Publication
Batcheldor GD, Giansanti JS, Hibbard ED, Waldron CA (1) Garrè's osteomyelitis of the jaws: a review and report of two cases *J Am Dent Assoc 1973;87:892-7* Ellis DJ, Winslow JR, Indovina AA (2) Garrè's osteomyelitis of the mandible. Report of a case. *Oral Surg Oral Med Oral Pathol. 1977 Aug;44(2):183-9* Marx RE (3) Chronic Osteomyelitis of the Jaws Oral and Maxillofacial Surgery Clinics of North America, Vol 3, No 2, May 91, 367-81	Garrè's osteomyelitis	Case report (1 & 2) Review article (3)
Perriman A, Uthman A Periostitis ossificans. Br J Oral Surg 1972; 10:211-6	Periostitis ossificans	Review article
Smith SN, Farman AG. Osteomyelitis with proliferative periostitis (Garrè's osteomyelitis). Report of a case affecting the mandible. *Oral Surg Oral Med Oral Pathol. 1977 Feb;43(2):315-8*	Osteomyelitis with proliferative periostitis	Case report
Eisenbud L, Miller J, Roberts IL Garrè's proliferative periostitis occurring simultaneously in four quadrants of the jaws. *Oral SurgOral Med Oral Pathol. 1981 Feb;51(2):172-8*	Garrè's proliferativ e periostitis	Case report
Panders AK, Hadders HN Chronic sclerosing inflammations of the jaw. Osteomyelitis sicca (Garrè), chronic sclerosing osteomyelitis with finemeshed trabecular structure, and very dense sclerosing osteomyelitis. *Oral Surg Oral Med Oral Pathol 1970 Sep;30(3):396-412*	Osteomyelitis sicca (synonymous osteomyelitis of Garrè, chronic sclerosing nonsuppurative osteomyelitis of Garrè, periostitis ossificans)	Review article
Mittermayer CH Oralpathologie. *Schattauer, Stuttgart-New York 1976*	Chronic osteomyelitis with proliferative periostitis (Garrè's chronic nonsuppurative sclerosing osteitis, ossifying periostitis)	Textbook
Schelhorn P, Zenk W [Clinics and therapy of the osteomyelitis of the lower jaw]. *Stomatol DDR 1989 Oct;39(10):672-6* Bernier S, Clermont S, Maranda G, Turcotte JY Osteomyelitis of the jaws J Can Dent Assoc 1995 May;61(5):441-2, 445-8	Chronic sclerosing osteomyelitis Garrè, Garrè's chronic sclerosing osteomyelitis (proliferative osteomyelitis)	Review article
Topazian RG Osteomyelitis of the Jaws. In Topizan RG, Goldberg MH (eds): Oral and Maxillofacial Infections. *Philadelphia, WB Saunders 1994, Chapter 7, pp 251-88*	Garrè's sclerosing osteomyelitis	Textbook

term “alveolar osteitis” (dry socket) is generally used in the medical and dental literature to describe an absence of invasion into the bone. It should therefore not be regarded as a form of osteomyelitis (Marx 1991). In alveolar osteitis the commonly advocated theory suggests a clot breakdown due to the release of fibrinolysins either from microorganisms or trauma. In both situations the bacteria remain on the surface of the exposed bone, and an actual invasion does not occur. Although not considered a true infection, alveolar osteitis may lead to acute or secondary chronic osteomyelitis once the bacterial invasion into the medullar and cortical bone has occurred and a deep bone infection has been established.

2.5.8.2 Osteoradionecrosis and Radioosteomyelitis

Radiotherapy is considered a major column in the treatment of head and neck malignancies. Despite recent advances in radiotherapy, such as using modern three-dimensional techniques, as well as hyperfractionation or moderately accelerated fractionation and consequent prophylactic dental treatment, osteoradionecrosis is still an observed condition in maxillofacial units.

Aside from its effect on the tumor cells, radiation also has serious side effects on the soft and hard tissues adjacent to the neoplasm. Mucositis, atrophic mucosa, xerostomia, and radiation caries are well-known side effects of head and neck radiotherapy. Because of its mineral composition, bone tissue absorbs more energy than soft tissues and is therefore more susceptible to secondary radiation. In cases where the bone is irradiated exceeding a certain local dose, osteoradionecrosis may develop, leading to marked pain in the patient and possible loss of bone leading to functional and aesthetic impairment.

Osteoradionecrosis was once considered an infection initiated by bacteria, which invaded the radiation-damaged bone; hence, the term “radiation-induced osteomyelitis” or radioosteomyelitis was commonly used. Marx (1983) conclusively identified this condition as a radiation-induced avascular necrosis of bone. He was able to demonstrate that radiation caused a hypoxic, hypocellular, and hypovascular tissue, leading to a spontaneous or trauma-initiated tissue breakdown. The result is a chronic nonhealing wound, susceptible to superinfection. As in florid osseous dysplasia and other bone pathologies, microorganisms are responsible for contamination and, if invasion occurs, secondary infection of the bone, resulting in osteomyelitis.

2.5.8.3 Osteochemonecrosis

The medical literature describes several drugs and substances that facilitate or induce conditions known as osteonecrosis of the jaws, such as corticosteroids and other cancer and antineoplastic drugs. Exposure to white phosphorous among workers in the matchmaking industry in the nineteenth century has led to unusual necroses of the jaws, which became known in the literature as phossy jaw or phosphorous necrosis of the jaw.

In the recent years bisphosphonate therapy has become a widely accepted mainstay of therapy in various clinical settings such as multiple myeloma, metastatic cancer therapy, and treatment of advanced osteoporosis. With the increased prescription of these drugs, the incidence and prevalence of bisphosphonate-associated complications of the jaw continues to be elucidated. This trend seems to be even more the case in patients receiving injectable bisphosphonates, such as pamidronate and zoledronic acid, but cases involving osteochemonecrosis of the jaw associated with chronic peroral administered bisphosphonates have also been reported (Ruggiero et al. 2004, 2006).

The pathophysiological mechanisms leading to bisphosphonate-induced osteochemonecrosis of the jaws are yet far from being fully understood; however, it seems apparent that important differences to the pathogenesis of osteoradionecrosis do occur (Hellenstein and Marek 2005). In bisphosphonate-induced osteochemonecrosis of the jaws osteoclastic action is reduced, but osteoblastic production continues, leading to an osteopetrosis-like condition (Whyte et al. 2003). These alterations in bone physiology with eventual increase of the medullary bone as the disease progresses and the inability of osteoclasts to remove superinfected “diseased” bone are regarded as causative factors. In contrast to osteoradionecrosis, where a radiation-induced avascular necrosis is the major cause, avascularity does not appear to be a major cofactor to date; however, inhibition of angiogenesis is currently being actively investigated (Fournier et al. 2002; Wood et al. 2002), and further research will hopefully help fully understanding its role in pathogenesis of this disease.

Regarding the current data and knowledge, we favor the term “bisphosphonate-induced osteochemonecrosis of the jaw” because it is not restricted to a certain pathogenesis. The term “bisphosphonate osteomyelitis” should not be used for the same reasons as the term radioosteomyelitis should be abandoned. The jawbone

with bisphosphonate-induced osteochemonecrosis is far more susceptible to bacterial invasion due to its strongly altered physiology; however, infection of the bone is to be considered a secondary phenomenon and not the primary cause of this disease entity.

2.6 Osteomyelitis of the Jaws: The Zurich Classification System

2.6.1 General Aspects of the Zurich Classification System

Osteomyelitis of the jaw as a clinical entity has long been recognized in the medical literature. As mentioned previously, various classification systems and nomenclatures of the disease have evolved with time. The heterogeneity of the classification systems is borne by the fact that several modalities are used to describe and define maxillofacial osteomyelitis. These modalities include etiology and pathogenesis, clinical presentation and course, radiology, and histopathology. Furthermore, most classification forms represent a mixture of these criteria, causing confusion, thereby hindering comparative studies.

At the Department of Cranio-Maxillofacial Surgery at the University of Zurich, the classification system for osteomyelitis of the jaws uses a hierarchical order of classification criteria. It is primarily based on clinical appearance and course of the disease, as well as on radiological features. Based on these criteria, three major groups of osteomyelitis can be distinguished:

1. Acute Osteomyelitis (AO)
2. Secondary Chronic Osteomyelitis (SCO)
3. Primary Chronic Osteomyelitis (PCO)

Within these major groups, the clinical presentation is similar in the majority of cases; however, as will be described later, a certain variety of the clinical course is noted, especially in cases of primary and secondary chronic osteomyelitis.

Histopathology is considered a secondary classification criterion, taking into account that findings are mostly unspecific and nonconclusive when considered by themselves; however, tissue examinations of biopsies are irreplaceable for confirmation of the diagnosis in cases of unclear and atypical clinical and radiological appearance, and moreover in excluding possible differential diagnosis.

Furthermore, in some cases of osteomyelitis with an atypical appearance a synthesis of medical history, clinical presentation, imaging studies, histopathology, and other diagnostic tools may be necessary to achieve an appropriate diagnosis.

Analysis of the osteomyelitis patients treated in the Department of Cranio-Maxillofacial Surgery in Zurich using the abovementioned major classification groups showed a clear predominance of cases diagnosed as secondary chronic osteomyelitis at the time of presentation, whereas cases of acute osteomyelitis and primary chronic osteomyelitis were significantly less often diagnosed (Table 2.6). In a small group of nine patients, despite meticulous work-up of all data including clinical course and symptoms, diagnostic imaging, laboratory

Table 2.6 Distribution of osteomyelitis cases treated at the Department of Cranio-Maxillofacial Surgery in Zurich, 1970–2000 (Baltensperger 2003)

Major groups of osteomyelitis of the jaws	Cases	
	N	%
Acute osteomyelitis (AO)	48	16.6%
Secondary chronic osteomyelitis (SCO)	203	70.0%
Primary chronic osteomyelitis (PCO)	30	10.3%
Not clearly classifiable/questionable osteomyelitis	9	3.1%
Total	290	100.0%

findings, and histopathology, no clear diagnosis was possible. Most of these cases showed a chronic course resembling primary chronic osteomyelitis or a (diffuse) sclerosing form of secondary chronic osteomyelitis. In some of these cases the diagnosis of osteomyelitis was even questionable. The problems in diagnosis of these challenging cases and possible related differential diagnosis are outlined later in this chapter.

Further subclassification of these major osteomyelitis groups is based on presumed etiology and pathogenesis of disease. These criteria are therefore considered tertiary classification criteria. These tertiary criteria are helpful in determining the necessary therapeutic strategies which may differ somewhat among the subgroups. The nature of these subgroups are outlined in more detail later in this chapter.

An overview of the Zurich classification of osteomyelitis of the jaws and the classification criteria are given in Fig. 2.2 and Table 2.7.

2.6.2 Acute Osteomyelitis and Secondary Chronic Osteomyelitis

2.6.2.1 Definitions

The basic terminology used in the Zurich classification of osteomyelitis of the jaws was promoted by Hugo Obwegeser, among others. The general principles of this classification system were described and published by E. Hjorting-Hanson, a former staff member at the Department of Cranio-Maxillofacial Surgery Zurich, in 1970. Hjorting-Hanson, as many other authors before and after him, gave an excellent description of the clinical and radiological picture of acute and secondary chronic osteomyelitis; however, he fell short of clearly defining at what stage an acute/subacute osteomyelitis should be considered chronic. To our knowledge, Marx (1991) and Mercuri (1991) were the first and only authors to define the duration for an acute osteomyelitis

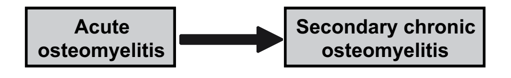


Fig. 2.2 The Zurich classification of osteomyelitis of the jaws: since secondary chronic osteomyelitis is a sequel of the prolonged and chronified acute form, both basically have the same subclassification groups

Table 2.7 Classification criteria upon which the Zurich classification of osteomyelitis is based

Hierarchic order of classification criteria	Classification criteria	Classification groups
First	Clinical appearance and course of disease Radiology	Major Groups Acute osteomyelitis (AO) Secondary chronic osteomyelitis (SCO) Primary chronic osteomyelitis (PCO)
Second	Pathology (gross pathology and histology)	Differentiation of cases that cannot clearly be distinguished solely on clinical appearance and course of disease; important for exclusion of differential diagnosis in borderline cases.
Third	Etiology Pathogenesis	Subgroups of AO, SCO, and PCO

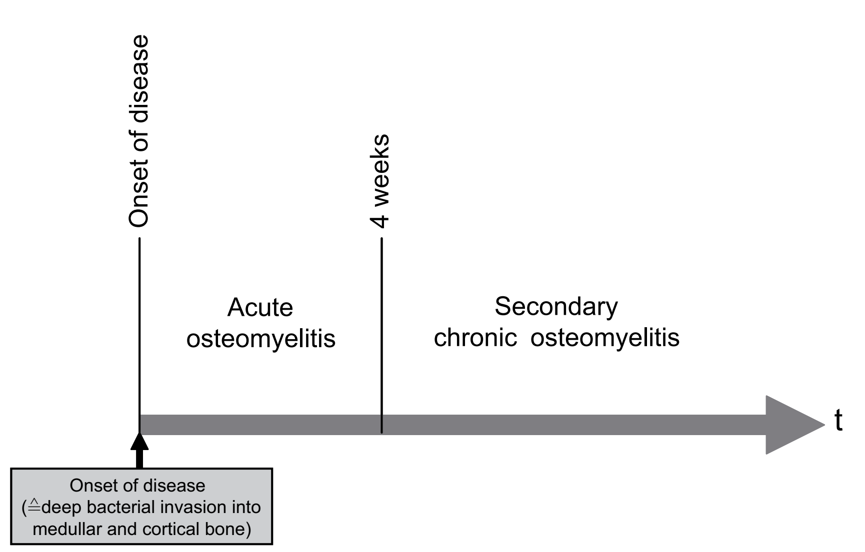


Fig. 2.3 Definition of acute and secondary chronic osteomyelitis of the jawbone (Adapted from Marx and Mercuri 1991)

until it should be considered as chronic. They set an arbitrary time limit of 4 weeks after onset of disease. Pathological–anatomical onset of osteomyelitis corresponds to deep bacterial invasion into the medullar and cortical bone. After the period of 4 weeks, a persisting bone infection should be considered as secondary chronic osteomyelitis (Fig. 2.3). Although the onset of the disease is a debatable point in time, it is still a simple and clear classification criterion and therefore of practical use for the clinician. This same definition was later used by several other authors (Eyrich et al. 1999; Schuknecht et al. 1997; Koorbusch et al. 1992). Because of its simplicity and clarity, this criterion is also used in the Zurich classification to differentiate acute osteomyelitis from secondary chronic osteomyelitis cases.

The term "subacute osteomyelitis" is not clearly defined in the literature. Most clinicians would probably agree that this term describes a condition somewhat in between acute and chronic osteomyelitis with relatively moderate symptoms. To avoid confusion and keep the classification as simple as possible, this term has been abandoned in the Zurich classification.

According to this definition, acute and secondary chronic osteomyelitis are to be considered the same disease at different stages of their course; hence, both groups are presented and discussed together in this chapter.

2.6.2.2 Predisposing Factors, Etiology, and Pathogenesis

2.6.2.2.1 General Considerations

As mentioned previously, there are several etiological factors, such as traumatic injuries, radiation, and certain chemical substances, among others, which may cause inflammation in the medullar space of the bone; however, acute and secondary chronic osteomyelitis, as these terms are generally used in the medical and dental literature and in this textbook, represent a true infection of the bone induced by pyogenic microorganisms.

The oral cavity harbors a large number of bacteria, among which many may be identified as possible pathogens to cause infection of the jawbone. Regarding the high frequency and sometimes severity of odontogenic infections in the daily dental and oral surgery practice, and the intimate relationship of dental roots apices with the medullar cavity of the jawbone, it is remarkable that osteomyelitis cases are not more frequently observed. Explanation for the low incidence of osteomyelitis of the jawbones can be explained by four primary factors which are responsible for deep bacterial invasion into the medullar cavity and cortical bone and hence establishment of the infection:

1. Number of pathogens
2. Virulence of pathogens
3. Local and systemic host immunity
4. Local tissue perfusion

Close interaction of these factors, as shown in Fig. 2.5, determine the pathological pathway of disease formation. In the healthy individual with sufficient host immunity mechanisms these factors form a carefully balanced equilibrium. If this equilibrium is disturbed by altering one or more of these factors, deep bone infection will be established (Figs. 2.4, 2.5).

2.6.2.2.2 Local and Systemic Host Immunity

The oral cavity, like no other part of the human body, is constantly exposed to various potential aggressors. Many of these bacteria, given the chance, may cause severe infection and damage to the tissue if they are not kept at distance. Due to its unique environment, many potent strategies have been developed to prevent deep tissue invasion of bacteria. Specific local immunological mechanisms, potent barrier systems, such as the periodontal membrane and a rich local vascular supply, are the most important. A more detailed description of these and other defense systems is provided extensively in specific literature and is beyond the scope of this book.

Every systemic disease with concomitant alterations in host defenses may influence profoundly the onset and course of acute and secondary chronic osteomyelitis. An alteration of some extent is probably the reason why osteomyelitis of the jaws develops in most cases, regardless of whether or not such deficiencies can be detected. Although the data is limited and lacks evidence-based criteria in most instances, osteomyelitis has been associated with a variety of systemic diseases and pathological conditions. A list of such diseases and conditions, as well their mechanisms, are given in Tables 2.8 and 2.9. In our retrospective study of 244 cases of acute and secondary chronic osteomyelitis of the jaws, alcohol and tobacco consumption were observed in 33.2 and 47.5% of the cases, respectively, while other conditions, as shown in Table 2.8, were only observed in a scarce number of patients (Baltensperger 2003); however, more important in this study than the mentioned systemic factors seemed to be the high prevalence of local infection in the examined patients with acute and secondary chronic osteomyelitis. Especially periodontal disease, which leads to a breakdown of the periodontal barrier membrane, facilitating deep invasion pathogens, seems to be an important condition leading to osteomyelitis. Significant periodontal disease was found in 51% of the patients of the same study.

It is important for the treating physician to consider host compromise and treat any compromising condition, when feasible, concomitantly with the infection.

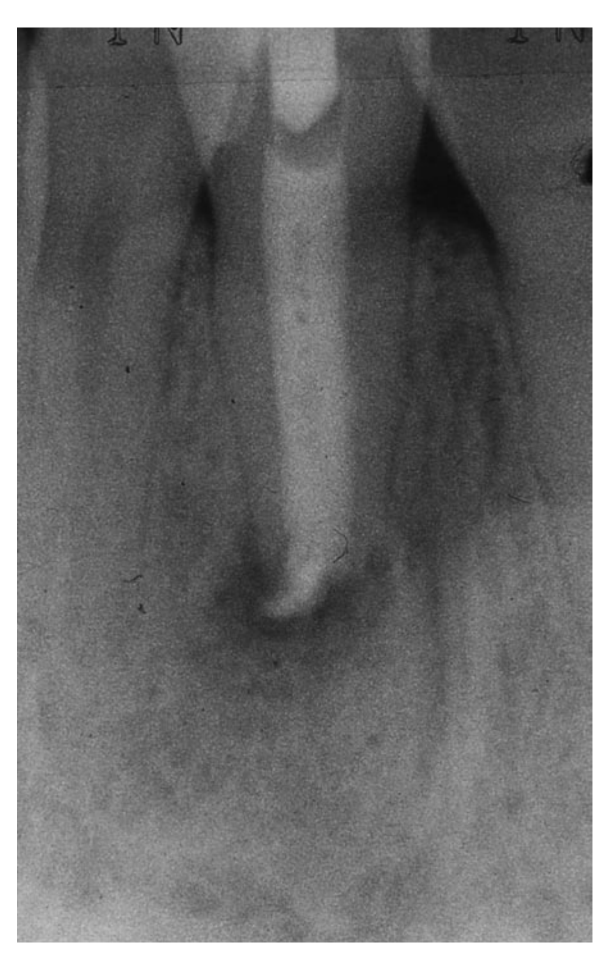


Fig. 2.4 Chronic infection of the periapical bone as a sequel of endodontic disease. This frequently observed condition represents a classical equilibrium between microbiological aggressors and host factors hindering further spread of the bacteria. If this balance is disturbed and shifts toward the side of the microorganisms, deep invasion into the medullar and cortical bone may occur and osteomyelitis is established

2.6.2.2.3 Local and Systemic Alterations in Bone Vascularity

Compromise of local blood supply must be considered a critical factor in the establishment of osteomyelitis. Systemic and local conditions that alter the vascularity of bone predispose the development of osteomyelitis. In these conditions immune cells and oxygen cannot reach the target area in an adequate manner. This facilitates the growth and spread of microorganisms, especially anaerobes, leading to establishment and progression of osteomyelitis. An overview of conditions compromising

blood supply of the jawbone is given in Table 2.10. In many cases of acute and secondary chronic osteomyelitis none of these factors may be apparent or detected; however, they must always be considered, looked for, and ultimately treated (Baltensperger 2003).

2.6.2.2.4 Microbiology

Acute and secondary chronic osteomyelitis are considered true infections of the bone induced by pyogenic microorganisms. As shown in Fig. 2.5, the number and virulence of these pathogens are important factors in the establishment of a bone infection.

Although until recently involvement of *S. aureus*, *S. epidermidis*, and *Actinomyces* were still discussed as the major pathogens in cases of osteomyelitis of the jaws, more recent studies favor the concept of a polymicrobic infection with several responsible pathogens. This shift in doctrine is explained mainly by modern, sophisticated culture methods, especially involving anaerobic media, which enable identification of possible pathogens more accurately. Consequently, many pathogens, which are mostly found in the healthy oral flora, have been associated with cases of jawbone osteomyelitis; however, prolonged antibiotic therapy prior to harvesting of the specimen and possible oral contamination complicate the interpretation of each result.

A more detailed overview and in-depth information on this topic is provided in Chap. 7.

2.6.2.2.5 Etiology and Pathogenesis, Subclassification Groups

According to the classification criteria stated previously, subclassification of acute and secondary chronic osteomyelitis is based on presumed etiology and pathogenesis of disease (Tables 2.7 and 2.11). Acute and secondary chronic osteomyelitis are initiated by a contagious focus of infection or by hematogenous spread. In osteomyelitis of long bones, hematogenous spread is the leading cause, especially in infants and children, because of the distinct anatomy of the metaphyseal region. In most of these cases a single responsible pathogen can be isolated (Mader and Calhoun 2000). *Staphylococcus* spp. are the most common organisms isolated in adults and are also prominent in children and infants.

Osteomyelitis of the jaws induced by hematogenous spread has become a rarity since the introduction of antibiotics; however, in regions of limited medical access these forms may still be noted. Especially one form of osteomyelitis of hematogenous spread merits special mention: neonatal or tooth-germ-induced acute osteomyelitis of the jaws. Because of its risks of involvement of the eye, spreading to the dural sinuses and creating loss of teeth and facial bone deformities if treated inadequately, this type of osteomyelitis should be remembered. Neonatal or tooth-germ-induced acute osteomyelitis occurs most often within the first few weeks after birth, affecting the upper jaw in most instances. This infection showed a mortality rate of up to 30% before the advent of an-

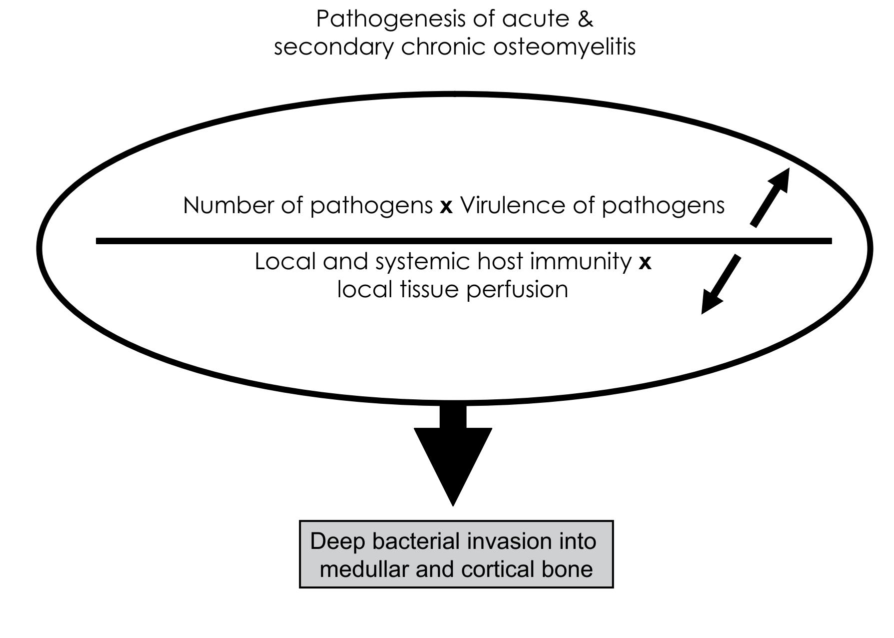


Fig. 2.5 Schematic illustration showing the interaction of host and pathogens. If the balance is shifted to the advantage of the aggressor, deep bone infection will be established (Modified after Marx 1999 and Mercuri 1999)

Table 2.8 Systemic host factors facilitating development of acute and secondary chronic osteomyelitis of the jawbone due to impairment of immune response mechanisms (Modified from Marx 1991; Mercuri 1991; Sanders 1978; Barbaglio et al. 1998; Battaglia et al. 1991; Bishop et al. 1995; Cheung et al. 1999; Exner et al. 1995; Groot et al. 1995; Hovi et al. 1996; Lawoyin et al. 1988; Melrose et al. 1976; Podlesh et al. 1996; Shroyer et al. 1991; Topazian 1994, 2002; Diktaban 1992; Koorbush et al. 1992; Eversole et al 1979; Meer et al. 2006)

Systemic factors altering host immunity	
• Diabetes mellitus • Autoimmune disorders • AIDS • Agranulocytosis • Anemia (especially sickle cell) • Leukemia • Syphilis	• Malnutrition • Chemotherapy • Corticosteroid and other immunosuppressive therapy • Alcohol and tobacco • Drug abuse • Prior major surgery • Herpes simplex virus (Zoster) and cytomegalovirus infection

Table 2.9 Mechanisms of systemic diseases/conditions predisposing to osteomyelitis (Adapted from Marx 1991)

Disease	Mechanism facilitating bone infection
Diabetes	Diminished leukocyte chemotaxis, phagocytosis, and lifespan; diminished vascularity of tissue due to vasculopathy, thus reducing perfusion and the ability for an effective inflammatory response; slower healing rate due to reduced tissue perfusion and defective glucose utilization
Leukemia	Deficient leukocyte function and associated anemia
Malnutrition	Reduced wound healing and reduction of immunological response
Cancer	Reduced wound healing and reduction of immunological response
Osteopetrosis (Albers–Schonberg disease)	Reduction of bone vascularization due to enhanced mineralization, replacement of hematopoietic marrow causing anemia and leukopenia
Severe anemia (particularly sickle-cell anemia)	Systemic debilitation, reduced tissue oxygenation, bone infarction (sickle cell anemia), especially in patients with a homozygous anemia trait
IV drug abuse	Repeated septic injections, spreading of septic emboli (especially with harboring septic vegetation on heart valves, in skin or within veins)
AIDS	Impaired immune response
Immunosuppression (steroids, cytostatic drugs)	Impaired immune response

Table 2.10 Host factors facilitating development of acute and secondary chronic osteomyelitis of the jawbone due to compromise of local blood supply (Modified from Marx 1991; Mercuri 1991; Sanders 1978; Barbaglio et al. 1998; Battaglia et al. 1991; Bishop et al. 1995; Cheung et al. 1999; Exner et al. 1995; Groot et al. 1995; Hovi et al. 1996; Lawoyin et al. 1988; Melrose et al. 1976; Podlesh et al. 1996; Shroyer et al. 1991; Topazian 1994, 2002; Diktaban 1992; Koorbush et al. 1992; Eversole et al 1979)

Local and systemic factors altering bone vascularity	
• Smoking • Diabetes mellitus • Florid osseous dysplasia • Fibrous dysplasia • Paget's disease • Osteopetrosis (Albers–Schonberg Disease)	• Osteoporosis • Bisphosphonate induced osteochemonecrosis • Other forms of osteonecrosis (mercury, bismuth, arsenic) • Tobacco • Radiation therapy and osteoradionecrosis • Bone malignancy (primary or metastatic)

tibiotics. The route of infection is considered by most clinicians to be hematogenous (Bass 1928; Lacey and Engel 1939; Heslop and Rowe 1956; Nade 1983), although a local infection caused by perinatal trauma of the oral mucosa and local trauma to the overlying mucosa of the alveolar ridge (Hitchin and Naylor 1957; Nade 1983; Topazian 1994, 2002), as well as extension of infection from adjacent teeth or soft tissues, are also discussed (Loh and Ling 1993). *Staphylococcus aureus* has been implicated as the organism responsible for this type of acute osteomyelitis (Asherson 1939; Haworth 1947; McCasch and Rowe 1953; Niego 1970; Nade 1983; Loh and Ling 1993).

The vast majority of cases of acute and secondary chronic osteomyelitis involving the jaws are usually caused by infection primarily spreading by a contagious focus. The most common foci are odontogenic, originating from infected pulp or periodontal tissue or infected pericoronal tissue from retained teeth, especially third molars.

Trauma, especially compound fractures, is also a major condition, which if not treated or treated inadequately, facilitates the development of osteomyelitis. But also every type of jawbone surgery, including surgical removal of impacted third molars, inevitably leads to a certain degree of local trauma to the bone, which causes local ischemia and may facilitate deep invasion of bacteria into the medullar cavity; hence, osteomyelitis can be established. Especially additional trauma to a preexisting chronic local infection carries a great risk of causing deep bone infection. Foreign bodies as well as the various transplants and implants used in maxillofacial and dental surgery also may harbor microorganisms and hence facilitate further spreading to the surrounding bone.

Several types of bone pathologies and systemic conditions, as mentioned previously, influence local tissue perfusion and immunity and therefore are important cofactors in establishing bone infection. In rare cases, infections derived from periostitis after gingival ulceration, furuncles, and facial and oral lacerations may also be considered causative.

In some instances the etiology and pathogenesis remains unclear or can only be speculated. These cases are subclassified as "other" in the classification system proposed in this book.

A distribution of acute and secondary chronic osteomyelitis cases, according to their etiology and pathogenesis, and their subclassification, respectively, is given in Table 2.12.

The distribution of acute and secondary chronic osteomyelitis shows a clear predominance of the mandible. In our patient data from 251 cases of acute and secondary chronic osteomyelitis only 16 patients (6.4%) demonstrated involvement of the upper jaw, whereas in the vast majority of cases (n=235; 93.6%) the mandible was the infected bone (Baltensperger 2003). The different anatomy of maxilla and mandible is probably the most important factor explaining the distribution of osteomyelitis involving the jawbones. The maxillary blood supply is more extensive than in the mandible. Additional thin cortical plates and the paucity of medullary tissues in the maxilla preclude confinement of infections within the bone and permit dissipation of edema and pus into the soft tissues of the midface and the paranasal sinuses (Topazian 1994, 2002). Maxillary osteomyelitis with tooth exfoliation after herpes zoster reactivation and concomitant cytomegalovirus infection has recently gained attention based on a review of the literature and 27 previous reports of herpes zoster-induced jaw infections (Meer et al. 2006).

The mandible is like a squashed long bone which has been shaped in a U-form. Like all long bones there is a clear distinction of a medullary cavity, dense cortical plates, and a well-defined periosteum on the outer border of the cortical bone. The medullary cavity is lined by

Table 2.11 Subclassification of acute and secondary chronic osteomyelitis of the jaws

Subclassification of acute and secondary chronic osteomyelitis of the jaws
Induced by hematogenous spread:
Neonatal, tooth germ associated
Extension from a local infection:
Trauma/fracture related
Odontogenic
Foreign body, transplant/implant induced
Associated with bone pathology and/or systemic disease
Other

the endosteum, which, like the periosteum, is a membrane of cells containing large numbers of osteoblasts. Within the medullary cavity a large variety of cells, such as reticuloendothelial cells, erythrocytes, granulocytes, platelets, and osteoblastic precursors, are harbored, as well as cancellous bone, fat, and blood vessels. Bone spicules radiate centrally from cortical bone to produce a scaffold of interconnecting trabeculae (Copehaver et al. 1978). The architecture of mandibular cortical bone resembles that of other long bones. Longitudinally orientated haversian systems (osteons), each with a central canal and blood vessel that provide nutrients by means of canaliculi to osteocytes contained within lacunae. These canals communicate with adjunct haversian systems as well with the periosteum and the marrow space by Volkmann's canals, thus forming a complex interconnecting vascular and neural network that nourishes bone and enables bone metabolism, necessary for repair, regeneration, and functional adaptation.

Acute and secondary chronic osteomyelitis of the mandible affects most commonly the body of the mandible, followed by the symphysis, angle, ascending ramus, and condyle (Calhoun et al. 1988; Baltensperger 2003).

The compromise of local blood supply is the critical factor and final common pathway in the establishment of acute and secondary chronic osteomyelitis (Fig. 2.7). Wannfors and Gazelius (1991) demonstrated by means of laser Doppler flowmetry (LDF) that long-standing local inflammation of the mandible was associated with a persistent reduction in blood flow.

Except for the coronoid process, which is supplied primarily from the temporalis muscle and the mandibular condyle, which is supplied in part by vessels from the lateral pterygoid muscle and the temporomandibular joint (TMJ) capsule, the major blood supply of the rest of the mandible consists of the inferior alveolar artery (Fig. 2.6). A secondary source is provided by the vessels of the periosteum. These vessels are organized in a reticular manner and run alongside of the cortical surface, giving off small nutrient vessels that penetrate the cortical bone and anastomose with branches of the inferior alveolar artery (Fig. 2.6; Castelli 1963; Cohen 1959); however, the value of the periosteal circulation probably cannot be seen as full replacement of the vascular supply of the marrow space. Hence, despite this adjunctive vascularization of the mandible through the periosteum, the main blood supply is derived from the inferior alveolar artery which, especially in elderly patients, is a vessel of small caliber and most susceptible to damage. This context can be transferred to the clinical appearance of osteomyelitis of the mandible, where occlusion of the inferior alveolar artery inevitably boosts the progress of the infection even if an intact periosteum is still present.

In most incidences periapical and periodontal infections are localized by a protective pyogenic membrane or soft tissue abscess wall which serves as a certain barrier (Schroeder 1991). As mentioned above, this condition represents a carefully balanced equilibrium between microorganisms and host resistance preventing further spreading of the infection. If the causative bacteria are sufficient in number and virulence, this barrier can be destroyed. Furthermore, permanent or temporary reduction of host resistance factors for various reasons mentioned previously facilitate deep bone invasion

Table 2.12 Etiology and pathogenesis of acute and secondary osteomyelitis cases treated at the Department of Cranio-Maxillofacial Surgery in Zurich, 1970-2000, according to Baltensperger (2003)

Subclassification groups of acute and secondary chronic osteomyelitis	Cases	
	N°	%
Induced by hematogenous spread	2	0.80
Neonatal, tooth germ associated		
Extension from a local infection		
Trauma/fracture related	42	16.73
Odontogenic	173	68.92
Foreign body, transplant/implant induced	13	5.18
Associated with bone pathology and/or systemic disease	5	1.99
Other	16	6.37
Total	251	100.00

of the microorganisms. This invasion induces a cascade of inflammatory host responses causing hyperemia, increased capillary permeability, and local inflammation of granulocytes. Proteolytic enzymes are released during this immunological reaction creating tissue necrosis, which further progresses as destruction of bacteria and vascular thrombosis ensue. Accumulation of pus inside the medullary cavity, consisting of necrotic tissue and dead bacteria within white blood cells, increases intramedullary pressure. This leads to vascular collapse, venous stasis, thrombosis, and hence local ischemia (A in Fig. 2.7; Topazian 1994, 2002). Pus travels through the haversian and nutrient canals and accumulates beneath the periosteum, elevating it from the cortical bone and thereby further reducing the vascular supply (B in Fig. 2.7; Topazian 1994, 2002). Elevation of the periosteum is usually observed more extensively in children, presumably because the periosteum is less firmly attached to the cortical bone than in adults. When pus accumulates continually underneath the periosteum, perforation may occur, leading to mucosal and cutaneous abscesses, and fistulas may develop.

In mandibular osteomyelitis, the increased intramedullary pressure also leads to direct compression of the neurovascular bundle, accelerating thrombosis and ischemia resulting in dysfunction of the inferior alveolar nerve, known as Vincent's symptom. The mandibular canal is also an anatomical pathway with no barrier function, alongside which pus can spread quickly (Fig. 2.8).

2.6.2.2.6 Chronification of Bone Infection

The chronification of the disease reflects the inability of the host to eradicate the pathogen due to lack of treat-

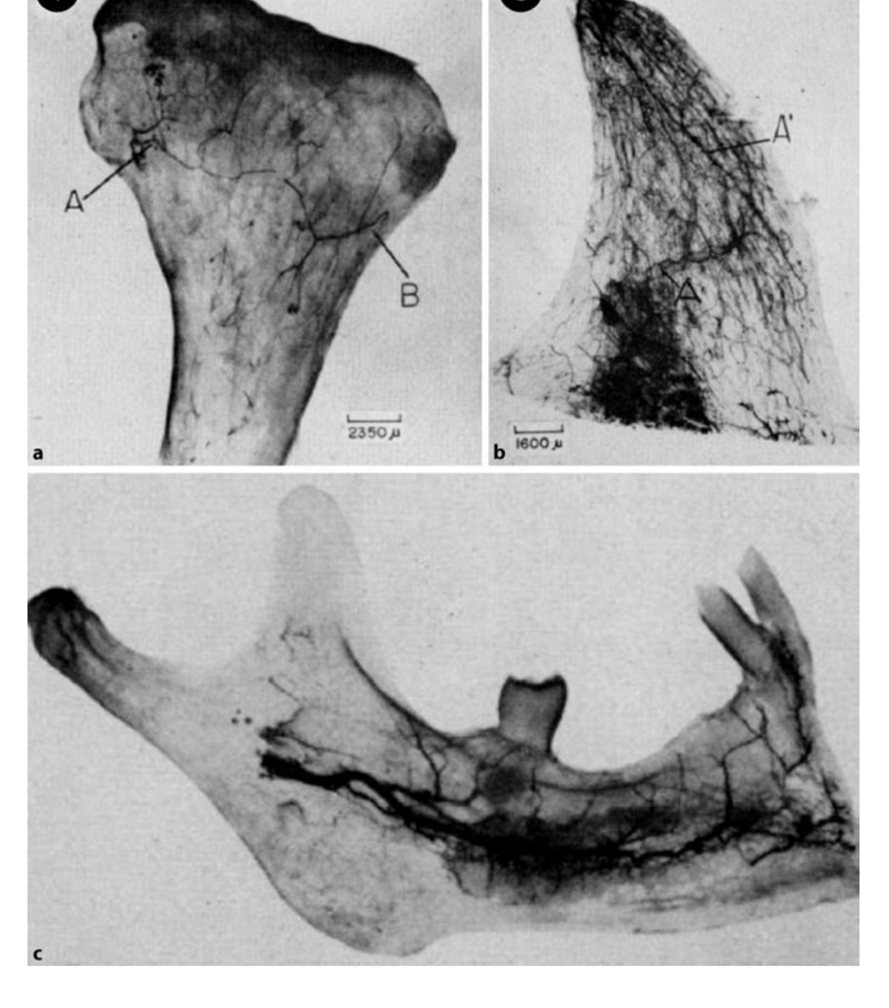


Fig. 2.6 **a** Condylar process arteries of an injected human head. Mandible soft parts were discarded after injection was performed through the common carotid artery. *A* artery coming from the lateral pterygoid muscle, *B* artery coming from vessels of the temporomandibular joint capsule (Teichmann's paste injection; decalcified and cleared). **b** Coronoid process arterial vessels. Two arterioles (*A* and *A'*) are present, both coming from the temporalis muscle (China-ink solution injection; decalcified and cleared). **c** Overall view of injected inferior alveolar artery (Teichmann's paste injection; decalcified and cleared). (From Castelli 1963)

ment or inadequate treatment, resulting in failure to reestablish the carefully balanced equilibrium between host factors and pathogens found in a healthy oral environment.

After the acute inflammatory process occurs and local blood supply is compromised, necrosis of the endosteal bone takes place. The bone fragments die and become sequestra (Fig. 2.9). Osteoclastic activity is then responsible for separating the dead bone from vital bone. Devital bone tissue clinically appears dirty, whitish-gray with an opaque appearance. Its fatty tissue has been destroyed and it does not bleed if scraped (Marx 1991). In some instances the bone sequester can demonstrate considerable dimensions (Fig. 2.10).

The elevated periosteum involved in the inflammatory process still contains vital cells. These cells, once the acute phase has passed, form a new bony shell (involucrum) covering the sequester. The involucrum may be penetrated by sinuses called cloacae, through which pus discharges, elevating the periosteum or forming fistula. As chronification progresses this scenario may be repeated (Figs. 2.11, 2.12). The involucrum tends to hinder sequester from extruding, which perpetuates the process because the whole area is bathed in increasing amounts of pus unless treated promptly and adequately (Killey and Kay 1970).

In secondary chronic osteomyelitis of the jaws, eventually a new equilibrium is established between the host and the aggressor causing the infection. The nature of this newly formed equilibrium is dependent on host immunity supported by medical therapy and the causative bacteria. It dictates the further course of the infection:

- If adequate therapy is administered on time, balance is shifted in favor of the host, resulting in complete healing of the infection.
- If no or inadequate therapy is provided, the disease may progress slowly or faster depending on the number and virulence of the bacteria and the remaining host defenses.
- If the number and virulence of the bacteria are small, host mechanisms may overwhelm, but still fail to fully eradicate the pathogen. In these instances a strong and diffuse sclerosis of the bone with or without a significant periosteal reaction can be noted. The clinical and radiological picture may then resemble primary chronic osteomyelitis.

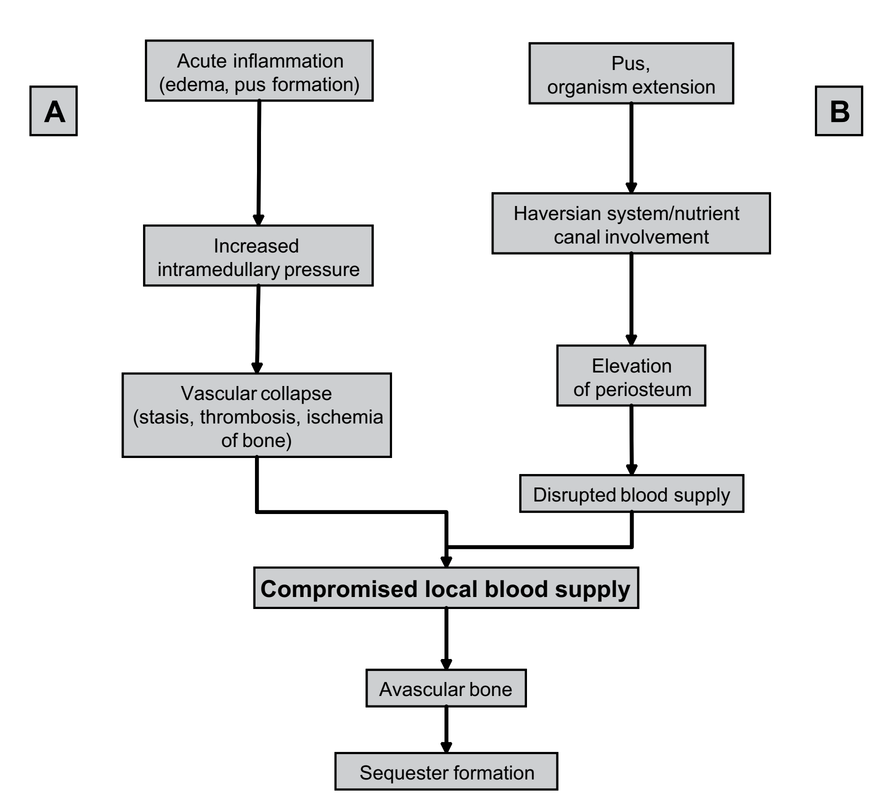


Fig. 2.7 Pathogenesis of acute and secondary chronic osteomyelitis of the jaws. Pathway *A* shows the role of inflammation and pathway *B* the role of pus formation in compromising blood supply of the infected bone, which can be considered as the final common pathway in the formation of sequestra (Modified from Topazian 1994, 2002)



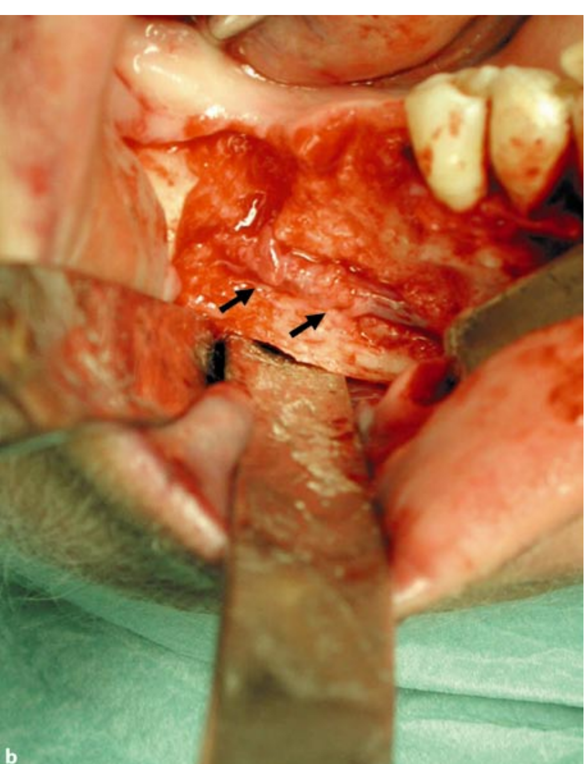
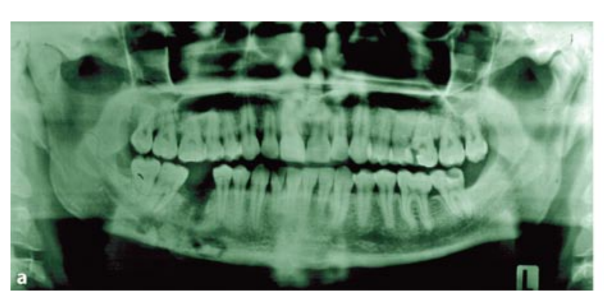


Fig. 2.8a,b Patient with acute osteomyelitis, beginning secondary chronic osteomyelitis of the right mandible following extraction of the lower right second molar. Her chief complaint was a marked hypoesthesia of the right inferior alveolar nerve (Vincent's symptom), which was documented preoperatively in **a**. **b** The intraoperative view after removal of the buccal cortical plate by decortication: note the granulation tissue alongside the inferior alveolar nerve (*arrows*) as a primary pathway for spread of the infection. (This case is described in detail in Chap. 12, case report 4)



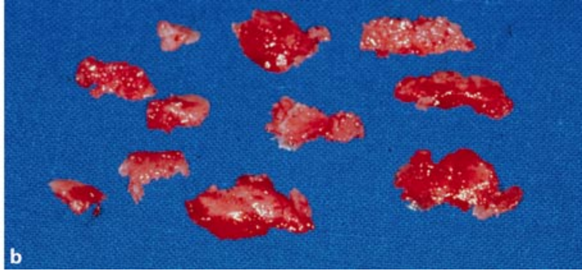


Fig. 2.9 **a** An OPG of a secondary chronic osteomyelitis case demonstrates osteolysis in the mandibular corpus around the alveolar region of the right first molar. A sequester is noted at the base of the right mandibular corpus with adjacent periosteal reaction. **b** Surgical specimen of the case shown in **a**: multiple sequesters and necrotic bone collected during debridement surgery

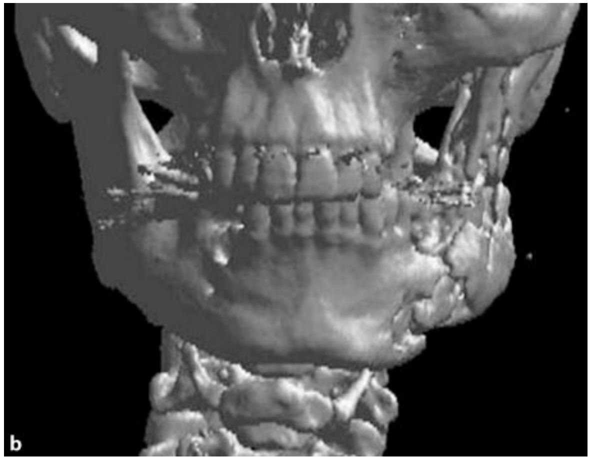
2.6.3 Clinical Presentation

2.6.3.1 Demographics

Acute and secondary chronic osteomyelitis may affect all ages and both sexes. In our retrospective analysis of 251 cases of acute and secondary chronic osteomyelitis there was a male predominance with a 2:1 ratio (Baltensperger 2003). Koorbush et al. (1992) described a male to female ratio of 3:1 in a survey of 35 patients. An equal gender distribution was noted by Daramola et al. (1982) in a larger African patient population.

The mean age of onset of disease in our studied cases was almost the same in cases of acute and secondary chronic osteomyelitis: 42.9 years (range 1–81 years) and 44.1 years (range 6–89 years; Baltensperger 2003), respectively. These figures are comparable with those described by previous investigators (Adekeye 1985; Calhoun 1988; Koorbush 1992; Daramola 1982).





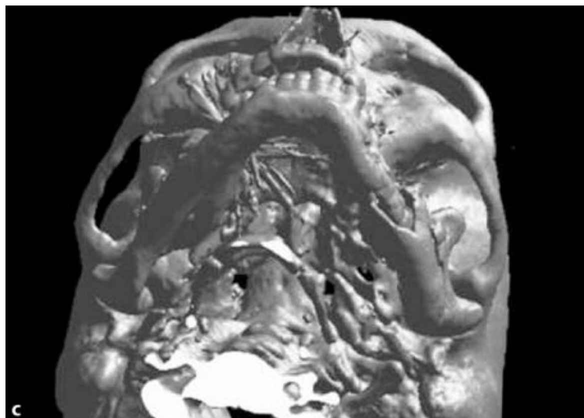


Fig. 2.10a–c The CT scans of a patient with secondary chronic osteomyelitis of the left mandible developing a giant sequester on the bases of the mandibular corpus. The progressive infection has weakened the bone and hence a pathological fracture has resulted. Sagittal CT scan (**a**) and 3D reconstructions (**b,c**). (Courtesy of N. Hardt)



Fig. 2.11 Axial CT scan of an extended secondary chronic osteomyelitis of the left mandible. A strong periosteal reaction with neoosteogenesis has formed an involucrum over several sequestra. (This case is described in detail in Chap. 12, case report 6)

2.6.3.2 Acute Osteomyelitis

The clinical appearance of acute osteomyelitis of the jaws may show a great variety, depending on the intensity of the disease and the magnitude of imbalance between the host and the microbiological aggressors. Three principal types of clinical courses of acute osteomyelitis can be distinguished:

- Acute suppurative
- Subacute suppurative
- Clinically silent with or without suppuration

Cases of acute osteomyelitis of the jawbone with an acute suppurative clinical course usually show impressive signs of inflammation. Pain can be intense and is mostly described by a deep sensation within the bone by the patient, which may be a valuable clue in the patient's history. Local swelling and edema due to abscess formation can also be substantial causing trismus and limitation of jaw function. The patients experiences a general malaise caused by high intermittent fever with temperatures reaching up to 39–40°C, often accompa-

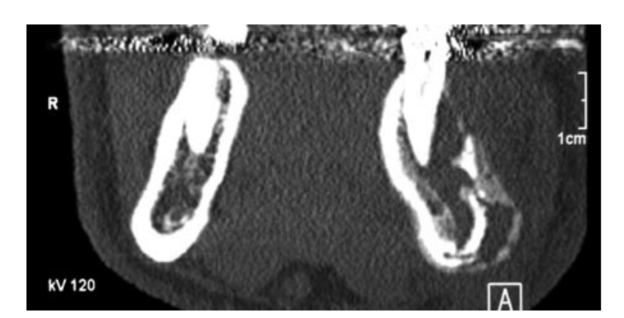


Fig. 2.12 Coronal view corresponding to axial CT scan shown in Fig. 2.11. (This case is described in detail in Chap. 12, case report 6)



Fig. 2.13 Acute odontogenic osteomyelitis with massive suppuration. Oral examination at initial presentation revealed pus in the sulci of the anterior incisors and canines on both sides, extending distally to the molars in the right lower jaw with multiple fistula formation

nied by regional lymphadenopathy. In some instances paresthesia or anesthesia of the lower lip is described (Vincent's symptom), indicating involvement of the inferior alveolar nerve. In most cases the cause of infection is odontogenic (Table 2.12) and can easily be identified. Pus may exude around the gingival sulcus and through mucosal and, possibly cutaneous, fistulas (Figs. 2.13–2.15). A fetid oral odor caused by anaerobic pyogenic bacteria often is present. Teeth in the affected region may demonstrate increased mobility even leading to malocclusion and show decreased or loss of sensitivity. Sequester formation and appositional neoosteogenesis are limited, if not absent, due to the short period since establishment of deep bone infection, which is the definition of acute osteomyelitis (Fig. 2.16).

Neonatal or tooth-germ-induced acute osteomyelitis of the jaws, as described previously, is a classical representative of this group, although this form of osteomyelitis has become a rarity in modern maxillofacial practice. But also in elderly patients this form of acute osteomyelitis has been seen much less frequently since the introduction of antibiotics and sophistication of medical and dental practice.

In cases of a subacute or silent course, with or without suppuration, the clinical presentation is by definition less impressive. This can make an early diagnosis increasingly difficult, and in many instances these cases are not detected until they have become secondary chronic.

An overview of symptoms at initial presentation of our patient data is given in Table 2.13.

2.6.3.2.1 Laboratory Findings

Depending on the intensity of the infection, laboratory results in acute osteomyelitis may demonstrate a wide range. While in cases with little inflammation the laboratory will only reveal moderate evidence of acute infection, cases which are accompanied by abscess formation will show more pronounced findings. Examination of our own patient data is demonstrated in Table 2.14.

2.6.3.3 Secondary Chronic Osteomyelitis

As a sequel of acute osteomyelitis, the clinical presentation of secondary chronic osteomyelitis of the jaws may also show a great variety, depending on the intensity of the disease and the magnitude of imbalance between the host and the microbiological aggressors and the time (Fig. 2.16). Following an acute or subacute clinical phase with suppuration, the chronification of the disease is reflected by the clinical course and findings. Most symptoms, such as pain and swelling, are usually less extensive in the chronic than in the acute stage. The deep and intense pain frequently observed in the acute stage is replaced by a more dull pain. Painful swelling caused by local edema and abscess formation in the acute stage is subsided by a harder palpable tenderness caused by periosteal reaction (see Figs. 2.11, 2.12). Other symptoms are somewhat more predominant in advanced stages, such as sequester and fistula formation, and are regarded as classical signs of secondary



Fig. 2.14 OPG at initial presentation (same patient as shown in Fig. 2.13). Osteolysis of the neighboring bone, derived from apical pathology, is noted in the incisor and canine region on both sides as well as in the molar region on the right side

chronic osteomyelitis (see Figs 2.10, 2.11, 2.12). The noted fetid odor often noted in cases of acute abscess formation is less frequent in patients with secondary chronic osteomyelitis. A disturbed occlusion can sometimes be noted when teeth of an affected region become more mobile and elongate due to rise of intraosseous pressure or a fracture present as a result or initiator of the osteomyelitic process.

An overview of symptoms at initial presentation of our patient data is given in Table 2.15.

In cases where the acute phase was clinically silent, secondary chronic osteomyelitis may begin as a hideous disease with little and somewhat unspecific clinical symptoms. In such instances the cause of the infection is considered to be a low-grade infection, which, however, cannot be fully eradicated by host defenses. These cases of secondary chronic osteomyelitis demonstrate less pus, fistula, and sequester formation, or may even lack these symptoms at a certain (progressive) stage of the disease. Furthermore, their radiological appearance may predominantly show a diffuse sclerosis with little to no osteolysis. Probably a large portion of the cases described in the literature as diffuse sclerosing osteomyelitis (DSO) falls into this category. A differentiation from primary chronic osteomyelitis may be difficult, if not impossible, in such cases (Figs. 2.17, 2.18); hence, it is most important to review the whole course of the disease and possibly obtain repeated imaging over time in such cases to establish the correct diagnosis.

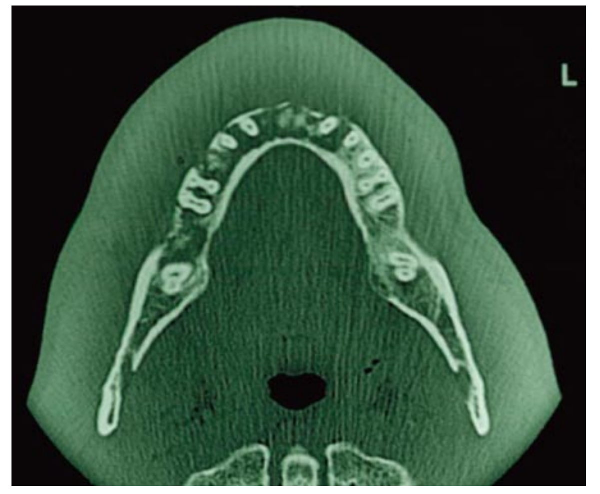


Fig. 2.15 Corresponding axial CT scan to OPG shown in Fig. 2.14 with a more detailed view of the osteolysis in the anterior and right sided alveolar bone

2.6.3.3.1 Actinomycotic and Other Rare Secondary Chronic Osteomyelitis of the Jaws

Specific clinical findings can be found in acute and especially in secondary chronic osteomyelitis caused by *Actinomyces*, *Nocardia*, and *Mycobacteria*. While *Actinomyces* is infrequently observed, the other pathogens are rarely associated with osteomyelitis of the jaws; however, if they are the causative pathogen, the clinical picture is somewhat atypical and hence deserves special recognition. In our studied cases we identified 5 patients with actinomycotic secondary chronic osteomyelitis, while osteomyelitis cases associated with *Nocardia* and *Mycobacteria* were not observed (Baltensperger 2003).

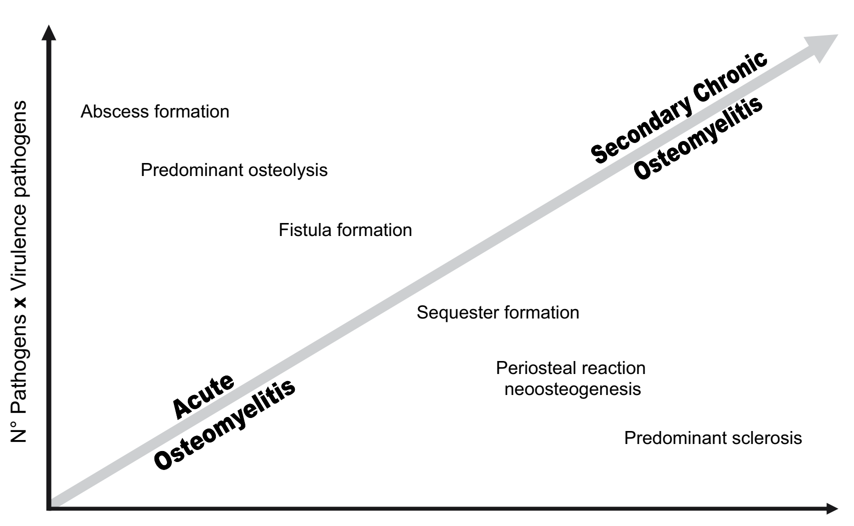


Fig. 2.16 Clinical and radiological features of acute and secondary chronic osteomyelitis of the jaws: the formation of certain clinical and radiological findings is dependent on the intensity of the disease and the magnitude of imbalance between the host and the microbiological aggressors, as well as the time frame

Table 2.13 Acute osteomyelitis: clinical symptoms at initial presentation at the Department of Cranio-Maxillofacial Surgery in Zurich (Baltensperger 2003)

Clinical Symptoms	Cases	
	N°	%
Pain	48	100.0
Swelling	43	89.6
Hypoesthesia[a]	25	52.1
Clinical abscess/pus formation	30	62.5
Extraoral fistula formation	0	0.0
Intraoral fistula formation	7	14.6
Sequester formation[b]	3	6.3
Exposed bone	3	6.3
Limited mouth opening	24	50.0
Lymphadenopathy	5	10.4
Fracture evident[c]	12	25.0
Myofacial, temporomandibular joint pain	1	2.1

[a]Hypoesthesia of the inferior alveolar nerve (Vincent's symptom)

[b]Only clinically diagnosed sequester formation without use of imaging

[c]Cases of trauma/fracture-related acute osteomyelitis

Table 2.14 Acute osteomyelitis: laboratory findings at initial presentation at the Department of Cranio-Maxillofacial Surgery in Zurich (From Baltensperger 2003)

	Cases	
	N°	%
Erythrocyte sedimentation rate		
Data available	23	100.0
Normal (♂ ≤15; ♀ ≤20)	4	17.4
Elevated (♂>15; ♀ >20)	19	82.6
C-reactive protein		
Data available	15	100.0
Normal (<5)	5	33.3
Markedly elevated (>50)	5	33.3
Moderately elevated (3–50)	5	33.3
Leukocyte count		
Data available	38	100.0
Normal (age 2–3 years: 6000–17000; age 4–12 years: 5000–13000; adults: 3800–10500)	23	60.5
Moderately elevated (age 2–3 years: 17000–20000; age 4–12 years: 13000–15000; adults: 10500-13000)	4	10.5
Markedly elevated (age 2–3 years: >20000; age 4–12 years: >15000; adults: >13000)	11	28.9
Body temperature		
Data available	43	100.0
Normal temperature (≤37°C)	20	46.5
Subfebrile temperature (37°–38°C)	17	39.5
Febrile temperature (≥38°C)	6	14.0

Table 2.15 Secondary chronic osteomyelitis: clinical symptoms at initial presentation at the Department of Cranio-Maxillofacial Surgery in Zurich (Baltensperger 2003)

Clinical symptoms	Cases	
	N°	%
Pain	178	87.7
Swelling	162	79.8
Hypoesthesia[a]	78	38.4
Clinical abscess/pus formation	117	57.6
Extraoral fistula formation	15	7.4
Intraoral fistula formation	27	13.3
Sequester formation[b]	30	14.8
Exposed bone	38	18.7
Limited mouth opening	42	20.7
Pathological fracture due to secondary chronic osteomyelitis	4	2.0
Lymphadenopathy	29	14.3
Pseudarthroses[c]	3	1.5
Fracture evident[c]	29	14.3
Myofacial, temporomandibular joint pain	6	3.0

[a]Hypoesthesia of the inferior alveolar nerve (Vincent's symptom)

[b]Only clinically diagnosed sequester formation without use of imaging

[c]Cases of trauma/fracture-related acute osteomyelitis

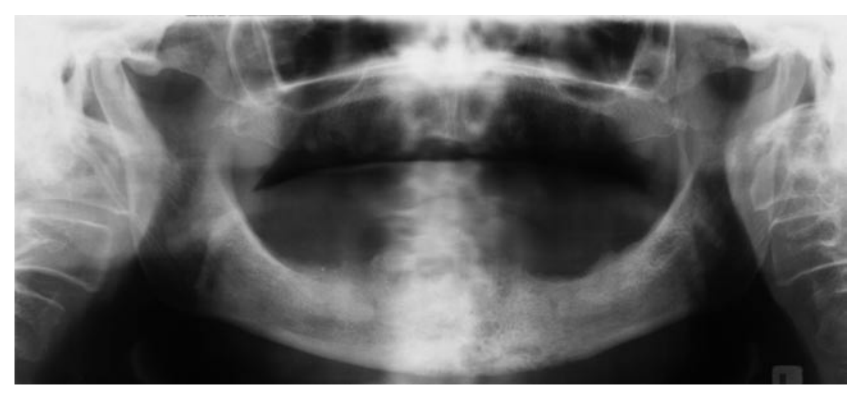


Fig. 2.17 Patient with secondary chronic osteomyelitis. After an initial phase of pus and fistula formation with local surgical drainage and prolonged antibiotic therapy, the process advanced with little clinical symptoms and demonstrated a diffuse sclerosing pattern of the left and right mandibular corpus and symphyseal region in the further course mimicking primary chronic osteomyelitis

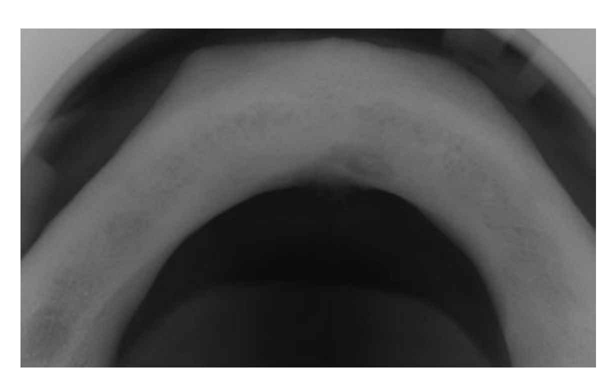


Fig. 2.18 Same as Fig. 2.17

Cervicofacial actinomycosis is a slowly progressive infection with both granulomatous and suppurative features. The disease predominantly affects the soft tissue of the head and neck with primary involvement of nearly every structure (Lerner 1988); however, in some instances the underlying bone, predominantly the mandible, can be infected by direct extension to the underlying bone or hematogenous spread (Topazian 1994, 2002).

As in most cases of secondary chronic osteomyelitis, infection with *Actinomyces* is mostly of endogenous origin, since the pathogen is known to be an oral saprophyte, present in periodontal pockets, carious teeth, tonsillar crypts, and other structures. Local infection, as well as surgical or nonsurgical trauma, facilitates penetration of the mucosal and periodontal barrier structures and allows penetration of deep tissue and bone (Bowden 1984). Advanced cervicofacial *Actinomycosis* spreads without regard for fascial planes and typically appears on cutaneous, rather than mucosal, surfaces.

Firm soft tissue masses are present on the skin with purplish to dark-red oily areas and occasionally small zones of fluctuance (see Fig. 9.1, 9.2, Chap. 9). Spontaneous drainage of serous fluid containing granular material may occur. When placed on a piece of gauze, these granular, yellowish substances, also called sulfur granules, can be seen clearly and represent colonies of bacteria (Topazian 1994, 2002). The underlying affected bone demonstrates the clinical and radiological picture of secondary chronic osteomyelitis with zones of osteolysis, delayed healing of extraction sites, and sclerosis on radiographs. Occasionally sequester formation is also noted.

Nocardiosis is also a chronic disease that may resemble actinomycotic infection. Although the primary target is usually the lungs, from where hematogenous spread leads the pathogen to other organs, the cervicofacial region, including bone, is occasionally involved (Schwartz and Tio 1987).

Tuberculosis is still a widespread infectious disease worldwide with also an increasing incidence again in countries with poor socio-economic conditions, concomitant with the AIDS pandemic. The etiology, pathogenesis, diagnosis, and treatment of tuberculosis are well described in other textbooks and are beyond the scope of this book.

Osteomyelitis of the jaws caused by infection with *Mycobacterium tuberculosis* is uncommon and, in most described instances, the tuberculosis infection is rarely confined to the bone. Adults are predominantly affected, although cases of affected children are also described (Bhatt and Jayakrishnan 2001; Hock-Liew et al. 1996; Kothari et al. 1998; Dimitrakopoulos et al. 1991; Fukuda et al. 1992). Oral tuberculous lesions are generally quite rare, despite the fact of high incidence of systemic involvement. A possible reason for this observation may be the inhibition of *Mycobacterium tuberculosis* by saliva and intact oral mucosa (Hock-Liew et al. 1996; McCarthy and Shklar 1980). The mechanisms of spread of infection are, in analogy to other osteomyelitis cases, caused by other bacteria, by direct inoculation, through tooth-extraction sockets, through any breach in the mucosa during tooth eruption, spread from adjacent soft tissue sites, or by hematogenous spread (Mishra and Bhoyar 1986). The clinical and radiological picture may resemble that of regular secondary chronic osteomyelitis with features similar to a dento-alveolar abscess; however, cervical lymphadenopathy, producing discrete or matted masses which are usually nontender, may be a distinctive presenting feature in some patients (Lee and Schecter 1995). This resemblance to conventional osteomyelitis cases underlines the importance of considering tuberculous osteomyelitis in the differential diagnosis of jaw lesions, especially if the patient's medical history is suspicious for possible infection (Bhatt and Jayakrishnan 2001).

Candida albicans has also been described as a potential microorganism to cause osteomyelitis in various bones of the skeleton, especially in conjunction with prosthesis. In the facial skeleton, however, documented cases of osteomyelitis caused by *Candida albicans* are extremely rare, despite the fact that *Candida* is known commensal of the oral cavity. Arranz-Caso

et al. (1996) report of a case of *Candida albicans* osteomyelitis of the zygomatic bone probably caused by self-inoculation of spores from muguet plaques on the oral mucosa to the exposed bone tissue by hand contact. The authors conclude that such a mechanism should be considered especially in patients who frequently have oral candiasis (e.g., diabetic, cancer, and HIV patients).

Cases of acute and secondary chronic osteomyelitis of the jaws have also been reported by bacteria which are rarely or not considered to be oral commensals. These cases, however, are extremely scarce, and hence the literature on these infections consists mainly of case reports.

2.6.3.3.2 Secondary Chronic Osteomyelitis Masquerading Malignancy

The clinical and radiological signs of secondary chronic osteomyelitis may share many similarities with malignancy complicated by secondary bone infection (Figs. 2.19, 2.20). This may lead to delay definite diagnosis and appropriate treatment in certain instances (Vezeau et al. 1990).

Lesions believed to be osteomyelitis that do not respond to treatment as expected within a short time should be viewed with concern. The patient's medical history, determining possible risk factors for developing oral carcinoma such as smoking, alcohol abuse, and poor oral hygiene, may be indicative, but imaging studies and representative biopsies should be performed to establish the diagnosis (Topazian 1994, 2002).

As much as the presence of a malignancy with invasion into the underlying jawbone may facilitate secondary infection, the opposite pathway may also be the case in rare instances. Ongoing bone infection may also lead to malignancy by neoplastic conversion of infectious tissue (Lemière et al. 2000; Niederdellmann et al. 1982).

2.6.3.3.3 Secondary Chronic Osteomyelitis Associated with Bone Pathology

As mentioned previously, there are several conditions which facilitate bone infection in the jaw. A summary of the most frequently involved pathological conditions enhancing the incidence of osteomyelitis of the jaws is given in Table 2.10; however, theoretically every pathological condition which alters bone physiology and/or vascularization of bone tissue may jeopardize host tissue defense mechanisms and hence may promote secondary infection. The unique location of the jawbones with their proximity to the heavily contaminated oral cavity makes them particularly vulnerable.

Depending on the nature of the underlying bone pathology, the clinical picture of succeeding secondary chronic osteomyelitis may differ from the average osteomyelitis infection established in "healthy bone." The initiation of infection is, like in regular acute and secondary chronic osteomyelitis, often a trauma such as extraction of a tooth or a dental infection leading to breakdown of the periodontal and/or mucosal barrier and promoting contamination and deep bone invasion of the jawbone. The further course of the disease is, however, strongly dependent on the reactive mechanisms of the host tissue (e.g., bone). In general, underlying bone pathology will reduce the defensive abilities of the host tissue and infection may spread faster than in healthy bone. Clinical and radiological signs reflecting suppurative infection, such as abscess and fistula formation, are similar to osteomyelitis cases without associated bone pathology. Bone reaction to infection, like osteolysis, sclerosis, sequester formation, and periosteal reaction, however, may strongly differ, making correct diagnosis and determining the extent of the infection more challenging (Fig. 2.21). In cases were necrotic bone is exposed to the oral cavity, secondary colonization of the bone and eventual deep bone invasion may occur (Fig. 2.22).

2.6.3.3.4 Laboratory Findings

In analogy to the clinical symptoms, the laboratory findings in secondary chronic osteomyelitis of the jaws are usually less prominent than in acute osteomyelitis. The overall moderate systemic reactions are reflected by these results and indicate a more localized infectious process, especially in secondary chronic osteomyelitis cases. This is especially true in cases with little or mild clinical symptoms where laboratory findings can be almost normal and hence are of little diagnostic or monitoring value. Examination of our own patient data is demonstrated in Table 2.16.

2.6.4 Primary Chronic Osteomyelitis

2.6.4.1 Definition

Acute and secondary chronic osteomyelitis of the jaw, as being the same disease at a different stage, share the same etiology, a bacterial or, in rare cases, a fungal infection. In the literature acute and secondary chronic

osteomyelitis are often summarized by the term "suppurative osteomyelitis," indicating a true bacterial infection with formation of pus.

The term "primary chronic osteomyelitis," as used in the Zurich classification of osteomyelitis of the jaws, refers to a rare inflammatory disease of unknown etiology. It is characterized as a strictly nonsuppurative chronic inflammation of the jawbone with the absence of pus formation, extra- or intraoral fistula, or sequestration. The absence of these symptoms represents a *conditio sine qua non* and clearly differentiates primary from acute and secondary chronic osteomyelitis in most cases. The term "primary chronic osteomyelitis" also implies that the patient has never undergone an appreciable acute phase and lacks a definitive initiating event.

The disease tends to a rise de novo without an actual acute phase and follows an insidious course. In most cases of primary chronic osteomyelitis, periodic episodes of onset with varying intensity last from a few days to several weeks and are intersected by periods of silence where the patient may experience little to no clinical symptoms. In active periods dull to severe pain, limitation of jaw opening and/or myofacial pain, as well as variable swelling, may be observed. In certain cases



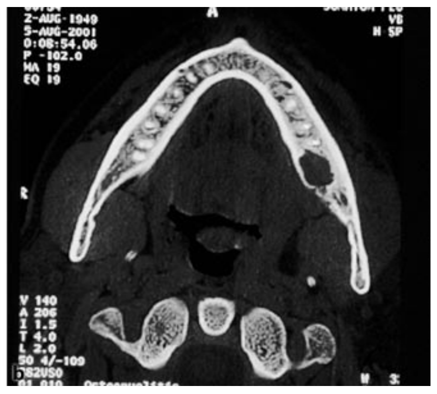


Fig. 2.19a,b Patient with a squamous cell carcinoma of the left lower jaw with concomitant secondary chronic osteomyelitis. The patient was referred to the maxillofacial unit approximately 1 month after surgical removal of the lower left second molar with chronic local fistula formation and pus discharge from the extraction site. The medical history, clinical appearance, and initial radiological work-up (OPG; Fig. 2.19 and corresponding axial CT scans in Fig. 2.20) were suspicious for secondary chronic osteomyelitis; however, initial bone and soft tissue biopsies revealed an invasive squamous cell carcinoma with a concomitant local bone infection

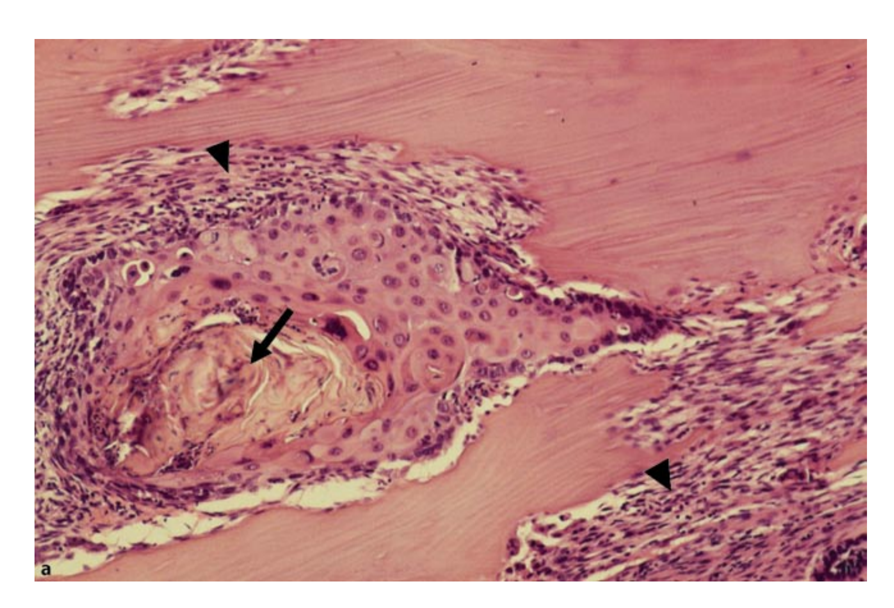


Fig. 2.20a,b Histology samples of the same patient shown in Figs. 2.19a and b. Hematoxylin and eosin stains. **a** Infiltration of bone by moderately differentiated squamous cell carcinoma. Keratinization in center of tumor cell islands (*arrow*). Peritumoral fibrosis and infiltration by inflammatory cells are present (*arrowheads*)

regional lymphadenopathy and reduced sensation of the inferior alveolar nerve (Vincent's symptom) are also accompanying symptoms.

Primary chronic osteomyelitis of the jaws almost always targets the mandible. In our patient data all but one case of primary chronic osteomyelitis involved exclusively the lower jaw. In the remaining case, the zygoma demonstrated the clinical, radiological, and histopathology findings as the mandible, indicating a possible spread of the pathological condition. The findings in the literature are similar to our data. Flygare et al. (1997) reported a case of primary chronic osteomyelitis with involvement of both jaws, which is considered to be a unique case.

2.6.4.2 Classification Problems of Primary Chronic Osteomyelitis of the Jaws

As mentioned previously, the classification of osteomyelitis of the jaws, and especially primary chronic osteomyelitis of the jaws, is somewhat confusing, mainly due to the wide variety of terms used to describe this disease entity. While diffuse chronic sclerosing or chronic sclerosing osteomyelitis are the favorite used terms in the

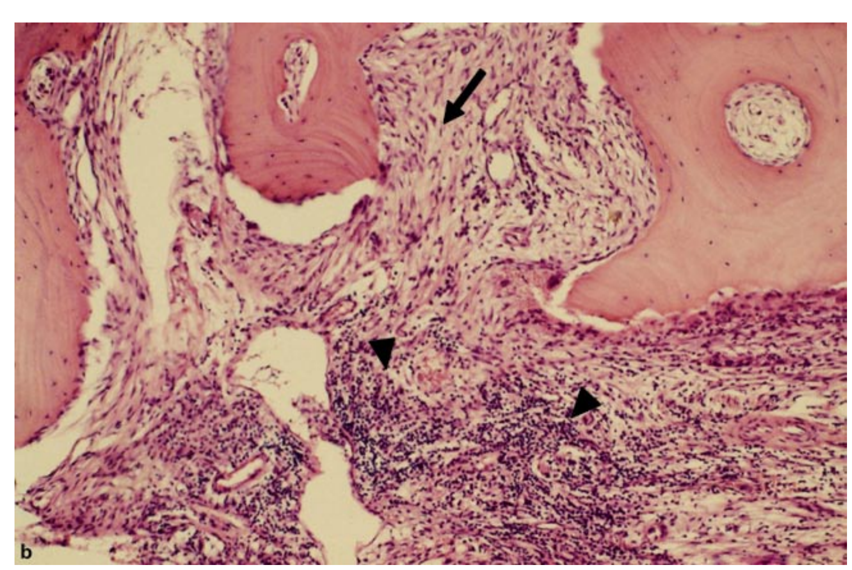


Fig. 2.20 (*continued*) Histology samples of the same patient shown in Figs. 2.19a and b. Hematoxylin and eosin stains. **b** Lamellar bone with preserved osteocyte nuclei is present besides signs of inflammation fibrosis of marrow spaces (*arrows*) and extensive infiltration by inflammatory cells (*arrowheads*)





Fig. 2.21 **a** A patient with a clinically extensive secondary chronic osteomyelitis of the frontal region with multiple fistula and abscess formations. The patient was treated with i.v. bisphosphonates for metastatic breast cancer. (This case is described in detail in Chap. 12, case report 10.) **b** A CT scan corresponding to **a**: The bone and periosteal reaction is not as strong as would have been expected from the clinical picture and compared with cases of secondary osteomyelitis of the mandible with no underlying bone pathology. (This case is described in detail in Chap. 12, case report 10)

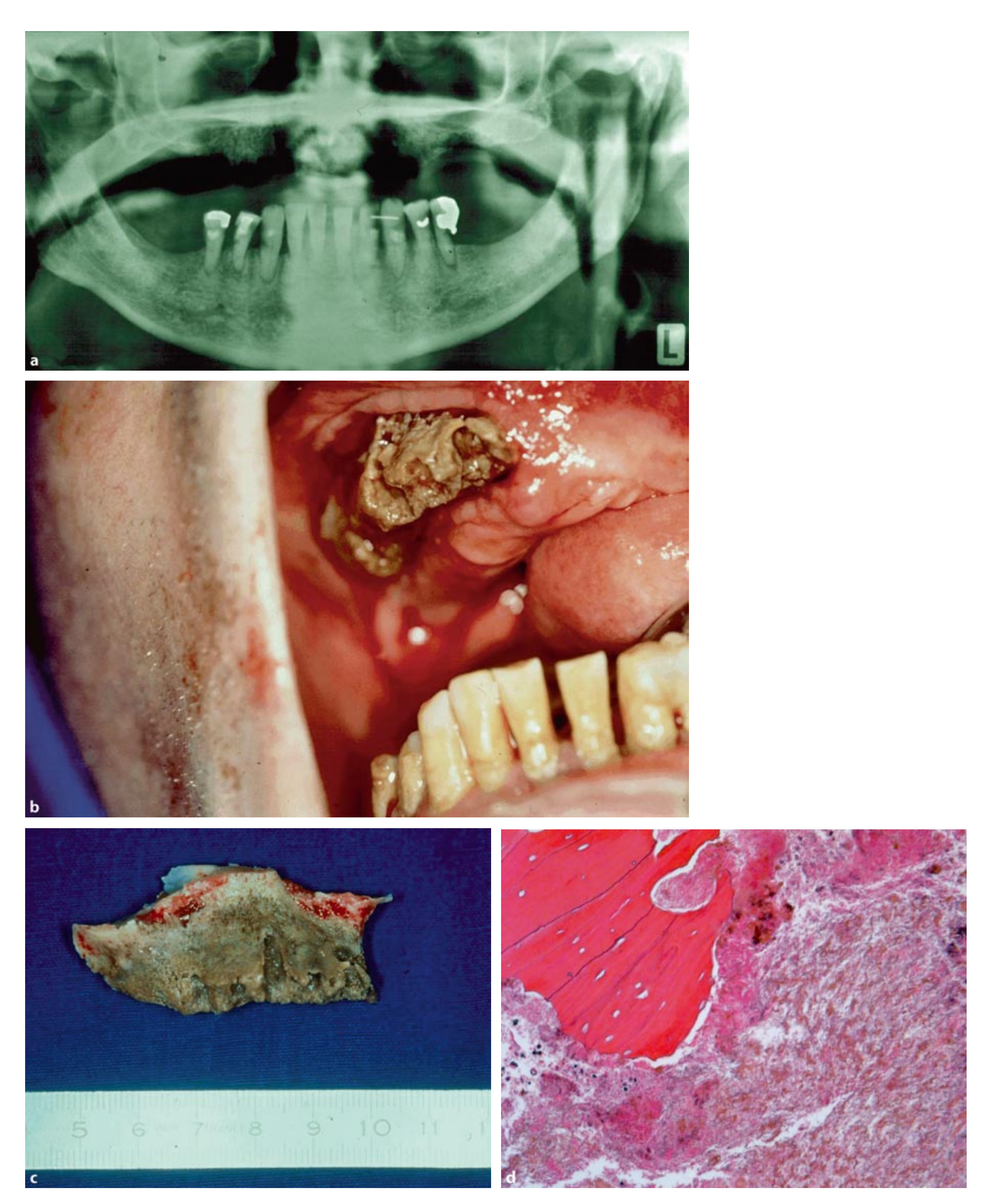


Fig. 2.22a–d Patient with CML and persisting necrotic bone in the upper right jaw after extraction of periodontal infected teeth with subsequent infection of the deep bone. **a** The orthopantomography and **b** the intraoral view at initial presentation of the patient. A large bone sequester was surgically removed (**c**). Histopathology demonstrates actinomyces (**d**; hematoxylin and eosin stain)

Table 2.16 Secondary chronic osteomyelitis: laboratory findings at initial presentation at the Department of Cranio-Maxillofacial Surgery in Zurich (From Baltensperger 2003)

	Cases	
	N°	%
Erythrocyte sedimentation rate		
Data available	124	100.0
Normal (♂ ≤15; ♀ ≤20)	54	43.5
Elevated (♂>15; ♀ >20)	70	56.5
C-reactive protein		
Data available	63	100.0
Normal (<5)	31	49.2
Moderately elevated (5–50)	18	28.6
Markedly elevated (>50)	14	22.2
Leukocyte count		
Data available	183	100.0
Normal (age 2–3 years: 6000–17000; age 4–12 years: 5000–13000; adults: 3800–10500)	135	73.8
Moderately elevated (age 2–3 years: 17000–20000; age 4–12 years: 13000–15000; adults: 10500-13000)	25	13.7
Markedly elevated (age 2–3 years: >20000; age 4–12 years: >15000; adults: >13000)	23	12.6
Body temperature		
Data available	193	100.0
Normal temperature (≤37°C)	133	68.9
Subfebrile temperature (37°–38°C)	56	29.0
Febrile temperature (≥38°C)	4	2.1

Anglo-American literature, primary chronic osteomyelitis is more often used by European authors; however, the list of terms used to describe primary chronic osteomyelitis is much longer. The terms used to describe this disease entity are often used falsely and interchangeably, and therefore comparing studies is difficult.

The review of our own patient data from the past 30 years (1970–2000) reflected the same classification problems seen in the literature with an inconsistent and often imprecise terminology used over the years (Baltensperger 2003). For instance, in 12 cases, the term diffuse sclerosing osteomyelitis (DSO) was used. While, after carefully reviewing the medical records, the final (revised) diagnosis was stated as primary chronic osteomyelitis in 9 of these cases, in the remaining 3 cases pus formation and/or presence of a fistula was observed at some point in the course of the disease, necessitating a change of the diagnosis to secondary chronic osteomyelitis. Similar nomenclature problems can be found in the medical literature. Suei et al. (1996) commented on a paper by Groot et al. (1996) that cases with "true DSO" were presented with suppuration and fistula formation. Using the classification advocated in this textbook, these cases would qualify as secondary chronic osteomyelitis. Hardt et al. (1987) presented a case report describing primary chronic osteomyelitis with fistula formation. The authors regarded this symptom, together with the presence of sequester, as part of primary chronic osteomyelitis, which they considered a suppurative infection of a vascular compromised bone (Hardt et al. 1987, Hardt 1991). Again, strictly following the Zurich classification, this case must be considered secondary chronic osteomyelitis.

In 11 cases of our patient data diagnosed as primary chronic osteomyelitis, the clinical course and symptoms clearly indicated a sclerosing course of secondary chronic osteomyelitis with formation of pus, fistula, or sequester formation at one stage of the disease (Baltensperger 2003). These cases of secondary chronic osteomyelitis with a predominant sclerosing character are particularly difficult, if not impossible, to distinguish from primary chronic osteomyelitis, if the disease is only viewed at a certain point in time and the whole course of the disease is neglected. Theoretically, a coincidence of primary chronic osteomyelitis with secondary chronic osteomyelitis may occur when a "superimposed" putrid bacterial infection is manifested in the impaired sclerotic bone. This, however, was never observed in our reviewed patient data, nor was, to our knowledge, such a case ever published.

Cases of osteomyelitis with a predominant periosteal reaction are in some instances falsely labeled as periostitis ossificans or Garrè's osteomyelitis. The nomenclature problems with the term "periostitis ossificans" (ossifying periostitis) and Garrè's osteomyelitis are discussed previously in this chapter.

Four cases in our patient data were given the diagnosis of periostitis ossificans (Garrè's osteomyelitis). A review of the medical records of these cases indicated that these were cases of primary chronic osteomyelitis. Other cases in the literature presented as Garrè's osteomyelitis must be considered to be secondary chronic osteomyelitis.

It must be emphasized again clearly that both terms, ossifying periostitis and diffuse sclerosing osteomyelitis, merely describe radiological features. Both primary and secondary chronic osteomyelitis may demonstrate these patterns with extensive sclerosis, variable amounts of osteolysis, and periosteal reaction on diagnostic imaging.

2.6.4.3 Subclassification of Primary Chronic Osteomyelitis of the Jaws

The diagnosis of primary chronic osteomyelitis can be difficult due to the insidious onset and course of the disease, which may demonstrate a great variety in its clinical and radiological appearance. The relatively rare incidence and the necessity for long and continuous observation periods are mainly responsible for the poor description of this disease entity in the literature. The reports on primary chronic osteomyelitis of jaws therefore all regard small patient groups or case reports.

Whereas the onset of the disease has been reported in all age groups, most published data refers to adults (Jacobson 1984; Van Merkesyn et al. 1988; Montonen et al. 1993). Scarce cases of primary chronic osteomyelitis with an onset in childhood and adolescence have mostly been presented as single case reports. Most of theses cases were described using the term Garrè's osteomyelitis (Panders and Hadders 1970; Ellis et al. 1977; Eisenbud et al. 1981; Mattision et al. 1981; Nortje et al. 1988; Betts et al. 1996; Heggie 2000).

To our knowledge, thus far only few authors have recognized age prevalence in the onset of primary chronic osteomyelitis. In our own patient data of 30 well-documented cases of primary chronic osteomyelitis of the jaws, the onset of the disease revealed two incidence peaks. An initial incidence peak was noted in adolescence (between 11 and 20 years) and a second (less

prominent) peak after age 50 years (Table 2.17; Baltensperger 2003; Baltensperger et al. 2004). A closer analysis of this patient data further revealed some differences in clinical appearance and course as well as in radiology and histopathology of these cases depending on the age of onset of the disease. Based on these differences the established major classification group, primary chronic osteomyelitis, was recently subclassified into early- and adult-onset primary chronic osteomyelitis, which shall be discussed in further detail (Fig. 2.2; Baltensperger et al. 2004).

Some patients with primary chronic osteomyelitis of the jaws demonstrate further osteomyelitic lesions in other parts of the skeleton with or without additional skin symptoms and affection of joints. The affection of the jaw is interpreted as part of syndrome in these patients and therefore described as syndrome-associated primary chronic osteomyelitis of the jaw in our proposed classification (Figs. 2.2, 2.23).

2.6.4.3.1 Adult-onset Primary Chronic Osteomyelitis

Adult-onset primary chronic osteomyelitis of the jaws describes cases with an onset of symptoms in the adult patient (e.g., after age 20 years; Tables 2.17, 2.18). The clinical symptoms of this disease are, as mentioned above, those of a chronic inflammation of the jawbone, excluding signs of suppuration. Principally, the clinically observed symptoms in the adult patient are the same as in the child or adolescent patient with primary chronic osteomyelitis of the jaws, with swelling and pain (ranging from dull to sharp) being the most often observed (Table 2.18, Fig. 2.24). A closer look of our reviewed cases revealed that the intensity of these symptoms were less prominent in adult-onset cases. Furthermore, symptoms tended to be less intense as the disease progressed. These results showed some correlation with radiological findings, which demonstrated more osteolytic findings and a greater periosteal reaction in cases of primary chronic osteomyelitis in children and adolescents compared with cases with onset in adult patients (Figs. 2.25, 2.26). Furthermore, a clear shift toward a more sclerotic pattern with normalization of the cortical architecture correlated somewhat in our patient data with clinical improvement. Similar findings were reported by other authors in cases of adult-onset as well as cases of early-onset primary chronic osteomyelitis (Van Merkestyn et al. 1988; Panders and Hadders 1970). These findings may be explained by the fact that radiological remission takes longer with extensive disease and patient age due to the general metabolic activity which decreases with age. In elderly patients residual sclerosis is more likely to persist.

An infection arising predominantly from a dental focus is the known etiology in cases of acute and secondary chronic osteomyelitis of the jaws. While an infectious etiology is also being discussed in primary chronic osteomyelitis, a chronic infection remains a readily discussed but still unproved hypothesis for this disease entity. Our patient data revealed two thirds of the patients (including six edentulous patients) with excellent oral health, making a dental focus unlikely (Baltensperger 2003; Baltensperger et al. 2004). The fact that long-term antibiotic therapy may ameliorate symptoms in primary chronic osteomyelitis patients supports this theory.

Jacobson et al. (1982) and Marx et al. (1994) identified *Propionibacterium acne*, species of *Actinomyces*, and *Eikenella corrodens* in patients with primary chronic osteomyelitis. However, these studies demonstrate some methodological deficits with possible contamination of specimens; hence, they cannot be seen as proof of the infectious hypothesis. Furthermore, according to the Henle-Koch postulates (Koch 1882), despite successful isolation of bacteria from a jawbone with primary chronic osteomyelitis, it is to date most difficult to grow microorganisms in pure culture and impossible to establish reinfection of a healthy host due to the lack of a susceptible animal model.

Our currently favored hypothesis, respecting results from our studies (Eyrich et al. 1999, 2000, 2003; Baltensperger et al. 2004) and the available literature on this subject, is that of a microorganism of low virulence functioning as a trigger that causes an exaggerated immune response in a genetically predisposed individual. The genetic predisposition may also be an explanation for wide variety and intensity of possible extragnathic manifestations seen in some patients with primary chronic osteomyelitis of the jaws, which is discussed later.

Basic immunological parameters in patients with primary chronic osteomyelitis of the jaws demonstrate a mild elevation of the erythrocyte sedimentation rate and the C-reactive protein level. These findings are usually accompanied by a normal leukocyte count. During onset and active periods of the disease, subfebrile body temperatures may be noted. In less active or silent periods of primary chronic osteomyelitis the body temperature was found to be normal (Baltensperger 2003; Baltensperger et al. 2004). Since primary chronic osteomyelitis shows a periodic course with active episodes followed by silent periods, an alteration in these basic immunological parameters which reflect the clinical

course seems reasonable; hence, observations of hyperactivity, hypoactivity, and even total impairment of immune response in patients with primary chronic osteomyelitis of the jaws are described (Jacobson et al. 1982; Malmström et al. 1983; Eyrich et al 1999).

In our examined patient data no differences regarding the basic immunological parameters were noted between adult- or early-onset cases, in cases with an associated SAPHO syndrome, or in cases of chronic recurrent multifocal osteomyelitis (Baltensperger 2003; Baltensperger et al. 2004).

2.6.4.3.2 Early-onset Primary Chronic Osteomyelitis (Juvenile Chronic Osteomyelitis)

Early-onset primary chronic osteomyelitis of the jaws describes cases with an onset in childhood or adolescence. Although most of the medical and dental literature dealing with primary chronic osteomyelitis of the jaws describes the disease in adult patients, in recent years the attention to cases in children and adolescents has grown. Our patient data revealed a first

Table 2.17 Primary chronic osteomyelitis: age at onset of symptoms (From Baltensperger 2003; Baltensperger et al. 2004)

Age at onset of symptoms (years)	Cases	
	N°	%
0–10	3	10
11–20	10	33
21–30	3	10
31–40	2	7
41–50	2	7
51–60	3	10
61–70	6	20
71–80	1	3
Total	30	100

Table 2.18 Primary chronic osteomyelitis (adult and early-onset cases): clinical symptoms prior to/at initial presentation (From Baltensperger 2003; Baltensperger et al. 2004)

Clinical symptoms	Cases	
	N°	%
Swelling	28	93
Pain	26	87
Limited mouth opening	17	57
Myofacial and/or temporomandibular joint pain	11	37
Hypoesthesia (Vincent's symptom)	9	30
Regional lymphadenopathy	7	23

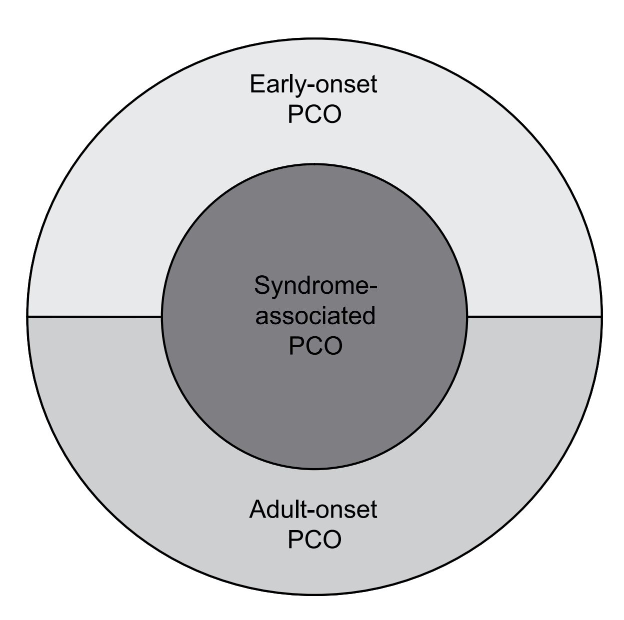
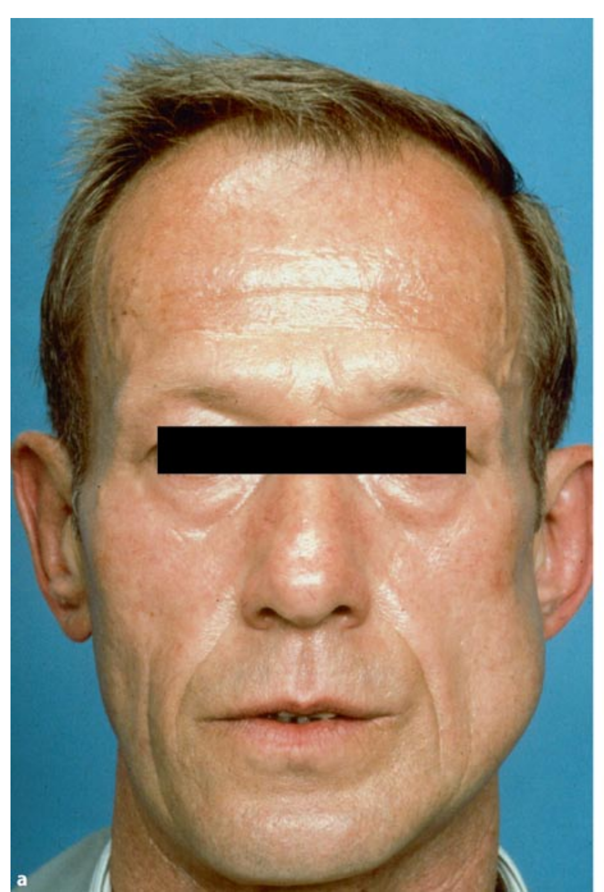


Fig. 2.23 Subclassification of primary chronic osteomyelitis of the jaws. The subclassification primarily differentiates the age of onset as a selective criteria. Cases of further extragnathic dermatoskeletal involvement are found in both groups of early- and adult-onset primary chronic osteomyelitis. These cases are additionally considered to be syndrome associated



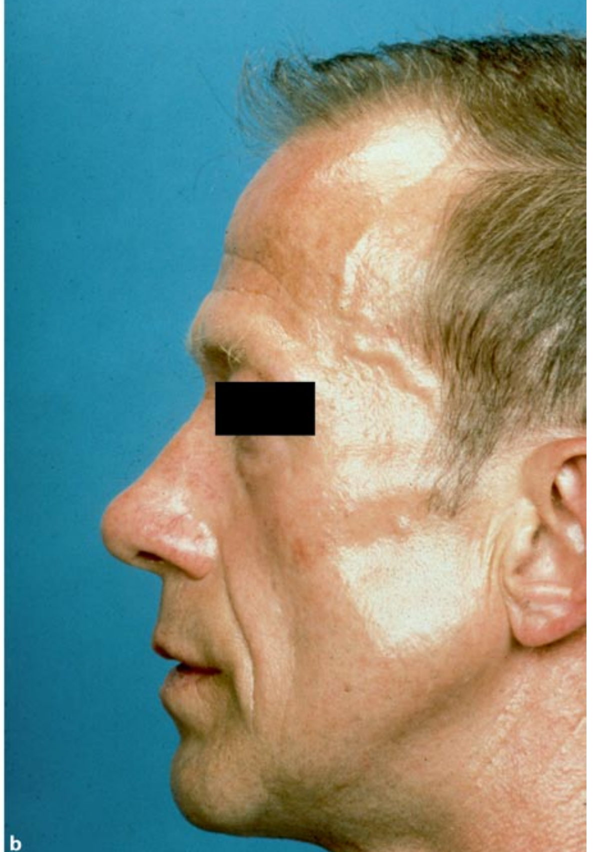


Fig. 2.24a,b A 51-year-old patient with adult-onset primary chronic osteomyelitis of the left mandible. Clinical symptoms at first presentation were a painful swelling of the lower left jaw and limited mouth opening (Baltensperger et al. 2004). (This case is described in detail in Chap. 12, case report 14)

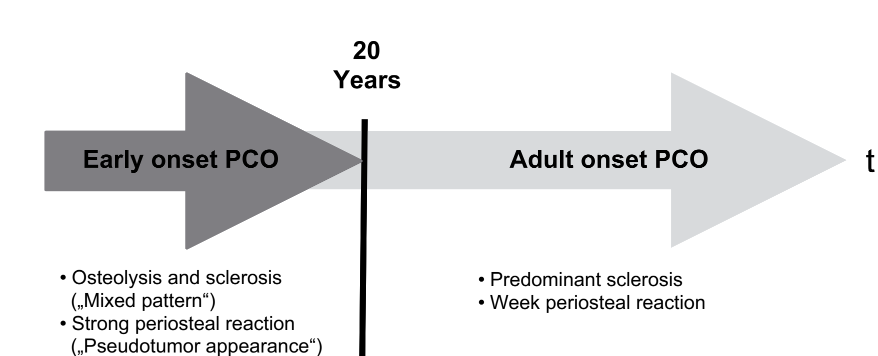
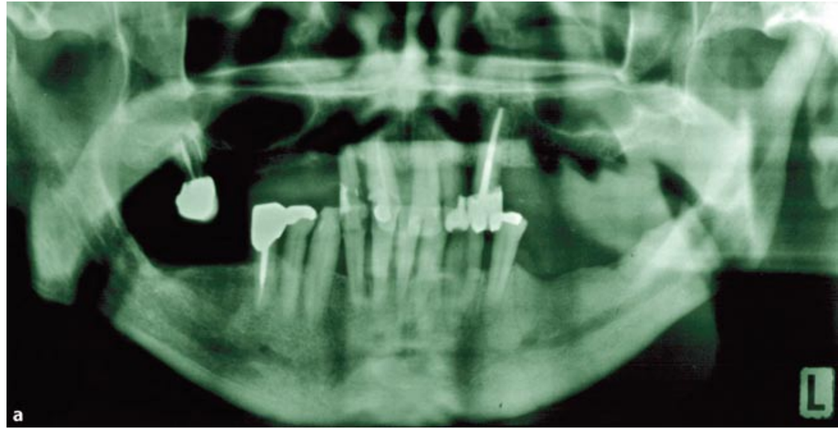


Fig. 2.25 The radiology of primary chronic osteomyelitis of the jaws (From Baltensperger 2003, 2004)



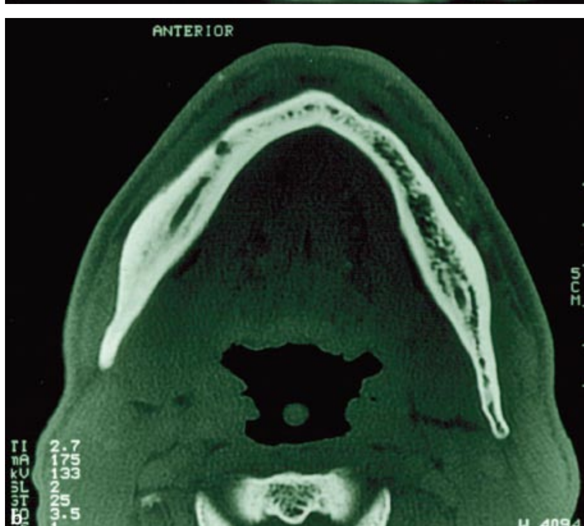




Fig. 2.26a-c An OPG, as well as axial and coronary CT scans, with adult-onset primary chronic osteomyelitis of the left mandible (same patient as shown in Fig. 2.24). Sclerosis is the predominant appearance with lack of osteolysis. The mandibular contours only demonstrate a mild thickening with a well-preserved anatomy (Baltensperger 2003, 2004). (This case is described in detail in Chap. 12, case report 14)

manifestation of primary chronic osteomyelitis in the first two decades in 13 of 30 reviewed cases (43%), with onset of one third of the cases in early to late puberty (Table 2.17; Baltensperger 2003; Baltensperger et al. 2004). To describe this patient group we have already used the term "juvenile chronic osteomyelitis" in recent publications (Eyrich et al. 1999, 2003; Baltensperger et al. 2004). This term was also used by Heggie and coworkers (2000, 2003) to describe their young patients with primary chronic osteomyelitis affecting the jaws.

The clinical symptoms of early-onset primary chronic osteomyelitis are generally the same in younger patients as in adults but usually of stronger intensity (Table 2.18). In active periods of the disease, the swelling and tenderness of the jaw is more prominent, due to a more extensive periosteal reaction (Jacobson 1984; Eyrich et al. 2003; Baltensperger 2003; Baltensperger et al. 2004). The swelling can create a voluminous expansion of the mandible with a pseudotumor-like appearance (Fig. 2.27). The radiological correlation of this pseudotumor is often a mixed pattern of small regions of osteolysis embedded in pronounced sclerotic bone. The periosteal reaction may lead to destruction of the cortical-marrow architecture and/or form an onion-like picture (ossifying periostitis), resembling osteosarcoma or other bone malignancies (Figs. 2.28, 2.29). In such instances a biopsy is the only possibility to rule out a malignancy.

The clinical course of early-onset primary chronic osteomyelitis can vary strongly. In some cases the active periods may become less intense as the patient outgrows puberty. This observation we made in our own patients led to the hypotheses that diminished bone growth, as seen after puberty, may play a role in the improvement of the disease (Eyrich et al. 2003). In other instances, however, a continuity of the disease was observed far into adulthood despite various therapeutic interventions. The lack of data on this rare disease makes it impossible to predict the clinical course and outcome in a given patient.

2.6.4.3.3 Syndrome-associated Primary Chronic Osteomyelitis

2.6.4.3.3.1 SAPHO Syndrome

The term SAPHO syndrome describes a chronic disorder that involves the skin, bones, and joints. SAPHO is an acronym that stands for morbid alteration of the dermatoskeletal system: synovitis; acne and pustulosis; hyperostosis; and osteitis. The clinical picture is determined by chronic inflammation of one tissue or a combination of any of these tissues. According to Kahn et al. (1994) three diagnostic criteria characterize SAPHO syndrome:

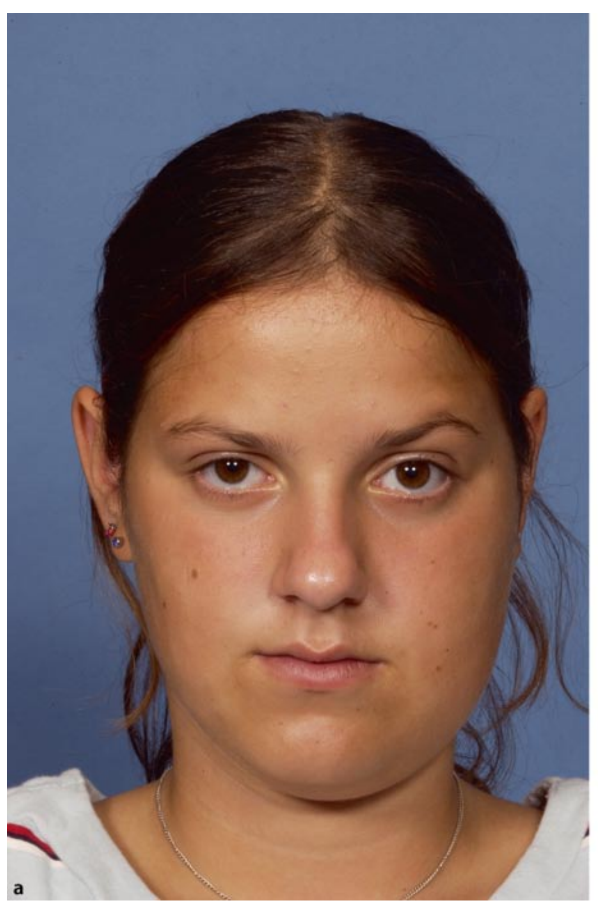
1. Multifocal osteomyelitis with or without skin manifestations
2. Sterile acute or chronic joint inflammation associated with either pustular psoriasis or palmoplantar pustulosis, acne, or hidradenitis
3. Sterile osteitis in the presence of one of the skin manifestations

The SAPHO syndrome was first described in 1986 by Chamot and coworkers. Since then, more than 50 terms referring to affections that may be observed in SAPHO syndrome patients have been described in the literature (Chamot and Kahn 1994), although many of these terms do not reflect the wide spectrum of diseases which characterize SAPHO syndrome. The main clinical pictures of SAPHO syndrome which must be seen as a nosological heterogeneous group are summarized in Table 2.19.

In the past two decades many authors have described a possible relationship between SAPHO syndrome and primary chronic osteomyelitis of the jaws (Brandt et al. 1995; Kahn et al. 1994; Garcia-Mann et al. 1996; Suei et al. 1996; Schilling et al. 1999; Eyrich et al. 1999; Roldan et al. 1999; Fleuridas et al. 2002). Kahn et al. (1994) and Suei et al. (1996) offered evidence that primary chronic osteomyelitis (described as DSO in their articles) was the mandibular localization of SAPHO syndrome. In fact, primary chronic osteomyelitis of the jaws with extramandibular involvement and skin lesion had already been described before the term SAPHO syndrome was popularized by Farnam et al. in 1984.

According to Kahn and Kahn (1994), one of the three criteria mentioned above is sufficient to establish the diagnosis SAPHO syndrome; however, definite diagnosis may be difficult and clinical, radiological, and histopathological data must be taken into account.

In some instances primary chronic osteomyelitis of jaws may precede other dermatoskeletal symptoms; in other cases it may follow other symptoms. It is therefore of the utmost importance for the physician treating patients with primary chronic osteomyelitis of the jaws to obtain a detailed history and full clinical examination in order to not overlook other possible symptoms indicating a possible SAPHO syndrome. Bone scans are very helpful in detecting extragnathic skeletal involvement,



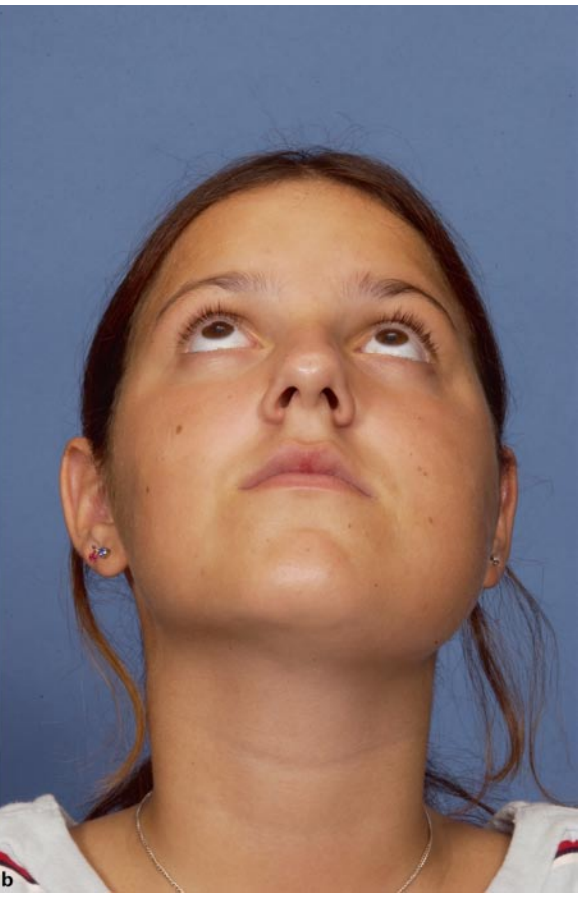


Fig. 2.27a,b A 16-year-old girl with early-onset primary chronic osteomyelitis involving the left mandible. On initial presentation there was a swelling of the left lower jaw accompanied by a dull pain in the same region. (This case is described in detail in Chap. 12, case report 16)



Fig. 2.28a–e Same patient as shown in Fig. 2.27. Photos taken at onset of the disease at age 16 years: OPG (**a**) and anteroposterior view (**b**) demonstrate volumetric expanse of the left mandible. **b** *see next page*





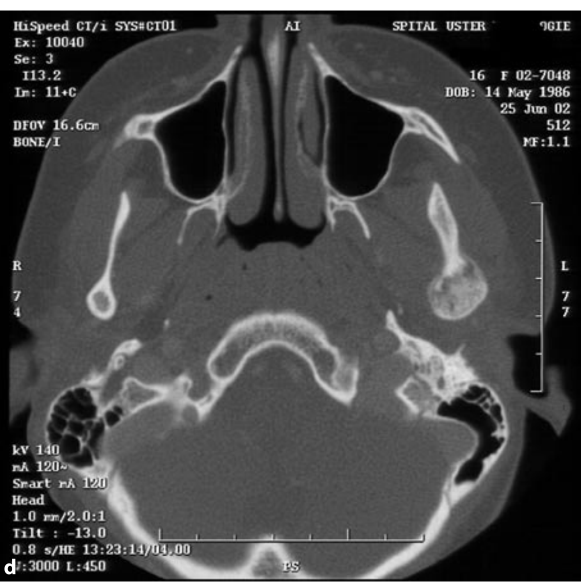




Fig. 2.28a–e (*continued*) Same patient as shown in Fig. 2.27. Photos taken at onset of the disease at age 16 years: OPG (**a**) and anteroposterior view (**b**) demonstrate volumetric expanse of the left mandible. The corresponding CT scans demonstrate a mixed pattern of predominant sclerosis intermingled with regions of osteolysis. The cortical-marrow architecture is dissolved. The 3D reconstruction of the mandible clearly shows the enlarged angle, ascending ramus, and condyle of the left mandible. (This case is described in detail in Chap. 12, case report 16)







Fig. 2.29a–c A 12-year-old boy with early-onset primary chronic osteomyelitis of the left mandible: note the onion-like pattern of the periosteal reaction (ossifying periostitis), which is seen in the OPG (**a**) and more clearly demonstrated in the axial and coronal CT scans (**b,c**). The corpus of the mandible and the ascending ramus further show a mixed pattern of sclerosis and osteolytic areas. (From Eyrich et al. 2003). (This case is described in detail in Chap. 12, case report 13)

which in some cases may be clinically silent. On the other hand, it is mandatory to rule out involvement of the jaws in every case of diagnosed SAPHO syndrome.

In our own patient data (Eyrich et al. 1999; Baltensperger 2003; Baltensperger et al. 2004), 8 patients with primary chronic osteomyelitis of the jaws were identified to also classify for the diagnosis SAPHO syndrome. The most prominent extragnathic symptoms we found were involvement of the sternoclavicular joint (Fig. 2.30) and palmoplantar pustulosis (Fig. 2.31). Although, as mentioned above, some radiological differences are age related, no specific radiological features were observed in our patient data in the syndrome-associated cases compared with cases from the same age group with no further dermatoskeletal involvement.

2.6.4.3.3.2 Chronic Recurrent Multifocal Osteomyelitis

Chronic recurrent multifocal osteomyelitis (CRMO) is an inflammatory disorder that mainly affects the metaphyses of the long bones, in addition to the spine, pelvis, and shoulder girdle; however, bone lesions are described at any site of the skeleton including the jaws. Because the lesions in CRMO patients affecting the mandible

Table 2.19 Main clinical pictures of SAPHO syndrome (Adapted from Schilling 2004)

Clinical picture of SAPHO syndrome
• Chronic recurrent multifocal osteomyelitis in children and adolescents
• Chronic recurrent multifocal osteomyelitis in adults
• Inflammatory anterior thoracic wall syndrome
• Acne + chronic recurrent multifocal osteomyelitis
• Triad: chronic recurrent multifocal osteomyelitis + Crohn's disease + palmo-plantar pustulosis
• Recurrent multifocal periostitis
• Pustulo-psoriatic hyperostotic spondylarthritis
• Sterno-costo-clavicular hyperostosis
• Acne + spondylarthritis
• Primary chronic osteomyelitis of the jaw

radiologically resemble cases of primary chronic osteomyelitis in the same age group, Suei et al. concluded that the latter may be considered the mandibular manifestation of CRMO (1995). Several publications in the past decade have postulated a possible nosological relationship between diffuse sclerosing osteomyelitis of the jaws (e.g., primary chronic osteomyelitis according to the classification used in this textbook) and chronic recurrent multifocal osteomyelitis (Reuland et al. 1992; Stewart et al. 1994; Suei et al. 1994, 1995; Flygare et al. 1997; Zebedin et al. 1998; Schilling et al. 1999).

Chronic recurrent multifocal osteomyelitis is usually characterized by periods of exacerbations and remissions over many years. Clinical diagnosis may be challenging because the clinical picture and course of the disease may vary significantly. Histological analysis of bone lesions in CRMO patients may help to differentiate them from other bone pathology, especially those which are malignant; however, they may resemble acute and secondary chronic osteomyelitis caused by microbiological infection. Therefore, an extensive microbiological work-up of the tissue biopsy, including PCR techniques, is essential in order to establish the diagnosis and hence decide on the treatment (Girschick 2002). As mentioned in Chap. 7, it is of the utmost importance to avoid contamination when harvesting a bone biopsy from a lesion for microbiological analysis. While lesions of CRMO in the mandible may be easier to access, an oral approach should be avoided for reasons mentioned previously. A biopsy from another part of the skeleton may therefore be of more diagnostic value, despite a possibly more invasive procedure to harvest the specimen.

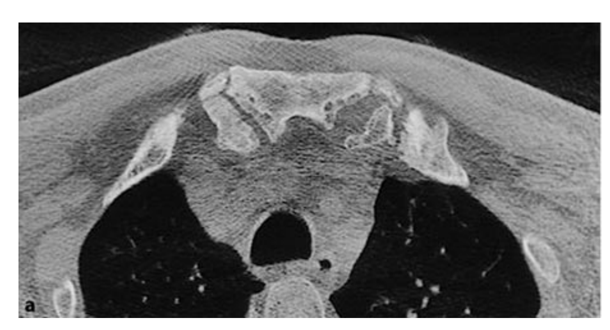
Chronic recurrent multifocal osteomyelitis is an extremely rare disease. No epidemiological data on incidence or prevalence have been published so far, although the incidence might be around 1:1,000,000, thus reflecting the number of patients followed-up (Girschick 1998, 2002).

The disease has been predominantly described in children, but cases in adults have also been noted but seem to be significantly less frequent than in the former group. Schilling and coworkers (2000) noted that with advancing age of patients with CRMO an increasing incidence of palmoplantar pustulosis (a part of SAPHO syndrome) is evident. Because of its possible relationship with other dermatoskeletal-associated diseases, CRMO has been integrated into the nosological heterogeneous SAPHO syndrome by several authors (Chamot et al. 1994; Schilling and Kessler 1998; Schilling et al. 2000).

2.7 Differential Diagnosis

2.7.1 General Considerations

The scope of possible differential diagnoses of osteomyelitis of the jaws may be extended by much other pathology affecting the jawbone that may mimic true bone infection in rare instances. To mention all of them is beyond the scope of this book. Only the most common diagnoses are briefly addressed in Chap. 3; however, it must be kept in mind that bone tissue is limited to react to a pathological stimulus. Bone may react with osteolysis or periosteal and endosteal reaction, resulting in bone apposition and expansive growth or sclerosis. It is therefore not surprising that a wide variety of pathology with different etiology leads to a similar clinical and radiological picture.



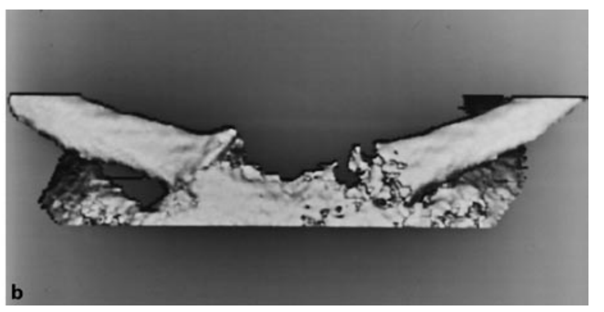


Fig. 2.30a,b Axial CT scan (**a**) and 3D reconstruction (**b**) in a patient with primary chronic osteomyelitis of the mandible with involvement of the sternoclavicular joints. The joints are characterized by cystic-osteolytic destructive lesions on the left side and hyperostosis on the right side. (From Eyrich 1999). (This case is described in detail in Chap. 12, case report 15)





Fig. 2.31a,b Typical plantar pustulosis (**a**) and palmar pustulosis (**b**). Note that due to localization of the lesion on the planta pedis, pustules are mostly disrupted with a local scaling of the skin. (Figure 2.31a from Eyrich 1999). (This case is described in detail in Chap. 12, case report 15)

2.7.2 Differential Diagnosis of Acute and Secondary Chronic Osteomyelitis

Most cases of acute and secondary chronic osteomyelitis are diagnosed readily by the clinical appearance and course of the disease, and the evaluation of diagnostic imaging (e.g., conventional and CT/MRI images, if necessary), and are therefore considered the primary criteria in the hierarchy of classification of osteomyelitis of the jaws (Table 2.7); however, in some instances the diagnosis may be difficult to impossible. As mentioned previously, some cases of secondary chronic osteomyelitis with a predominantly sclerosing course may mimic primary chronic osteomyelitis, especially if the disease is analyzed at one specific point in time (see Figs. 2.17, 2.18). Histological examination will probably not help to further differentiate these cases because of the resemblance (see Chap. 6).

Apical lesions are not yet considered to represent true osteomyelitis, since deep bone invasion is still lacking (Fig. 2.4); however, the transition to osteomyelitis may be insidious and thorough clinical and radiological work-up must be done once the diagnosis of osteomyelitis is considered. Cases of osteomyelitis may mimic a full-grown malignancy or be a sequel of a malignant tumor due to superinfection. On the other hand, certain bone tumors and other pathologies may appear clinically and radiologically as a bone infection; therefore, as a general rule, especially in unclear cases, it is necessary to confirm and rule out other possible differential diagnoses prior to definite therapy by histopathological confirmation.

A summary of the most frequent differential diagnoses of acute and secondary chronic osteomyelitis of the jaws is given in Table 2.20.

2.7.3 Differential Diagnosis of Primary Chronic Osteomyelitis

The clinical appearance and course of primary chronic osteomyelitis often makes a diagnosis more difficult compared with cases of acute and secondary chronic osteomyelitis. A predisposing event, such as an oral surgical procedure or an infectious tooth, is missing. More attention must be given to the patient's history in suspected cases. Due to the unspecific clinical symptoms, lacking clear signs of infection, such as pus or fistula formation, the list of differential diagnoses is somewhat different compared with acute and secondary chronic osteomyelitis.

A summary of the most frequent differential diagnoses of primary chronic osteomyelitis of the jaws is given in Table 2.21.

Florid osseous dysplasia (FOD) has often been confused with primary chronic osteomyelitis in the literature. As mentioned previously, this disease is an entity of its own. It may be seen, however, as a predisposing factor for bone infection. Florid osseous dysplasia appears on radiographs as sclerosing opaque and dense masses. The bone changes are often adjectant to the apices of the teeth and are restricted to the alveolar process in either or both jaws. Some cases of FOD occur in two phases. In the first phase, asymptomatic sclerotic masses develop. In the second phase inflammation is superimposed by bacterial invasion from periapical infection, advanced periodontal disease, extraction from teeth, attempts at surgical excision, or ulceration of mucosa when the lesions become superficial (e.g., when residual ridge resorption proceeds; Topazian 1994, 2002). Florid osseous dysplasia is diagnosed most often in black women, although cases are described in both genders and all races.

Florid osseous dysplasia may be difficult to distinguish from periapical cemental dysplasia (PCD), although the clinical course of FOD shows limited growth potential compared with PCD and does not produce pain, unless secondary infection occurs; however, in cases of PCD, bony sclerosis may extend from a localized periapical process to a regional lesion, mimicking more the picture of primary chronic osteomyelitis. While there may be some histological similarities between FOD and PCD, they are two distinct clinical entities and do not usually become more widespread. Periapical cemental dysplasia usually affects middle-aged women and is localized to the anterior mandibular teeth. The affected teeth always respond positively to vitality tests (Eyrich et al. 1999). The lesion presents in three typically distinct stages: osteolytic; cementoblastic; and inactive (Makek 1983).

An enostosis or compact island of bone can be observed as a dense sclerotic area of bone. This sclerotic area may be the result of an inflammatory process or trauma and is then referred to as a bone scar by some authors.

Osteoma, ossifying fibroma, osteochondrome, and other benign tumors of the jaws may also form distinct sclerotic masses, although they are usually clearly differentiated radiologically from primary chronic osteomyelitis; however, in some instances these lesions may be at the border of the jawbone and mimic periosteal reaction as seen in cases of primary chronic osteomyelitis.

Osteosarcoma is a malignant tumor that also affects the jaw. It may produce a growing bone mass causing dull pain. Especially cases of early-onset primary chronic osteomyelitis with a strong periosteal reaction, presenting with an onion-like appearance on radiographs (see Fig. 2.29), may mimic such a tumor, and only histology will confirm the diagnosis.

Patients with tendoperiostitis usually present with a history of parafunctional complaints. Palpation of the temporal, masseter, medial pterygoid and the digastric muscles, reveals tenderness in one or more of these locations (Van Merkesteyn et al. 1988). Radiographically, the picture may be very similar to primary chronic osteomyelitis with diffuse sclerosing of the marrow and the cortical plate in the absence of pus formation or sequestration.

Paget's disease is a disease of disturbed bone metabolism of unknown origin. It usually occurs in advanced age and affects the spine, pelvic skeleton, and cranial vault. Long bones and the facial skeleton are rarely involved. If the jaws are affected, the maxilla is somewhat more often involved than the mandible.

Osteopetrosis is a genetically inherited disease which involves all bones. Two major types are differentiated: an autosomal-recessive, malignant form with anemia which manifests at birth; and a autosomal-dominant, benign form. While the malignant form is more dramatic, with severe impairment and systemic complications and patients rarely living beyond the first decade of life, the benign form is more likely to be seen in daily practice.

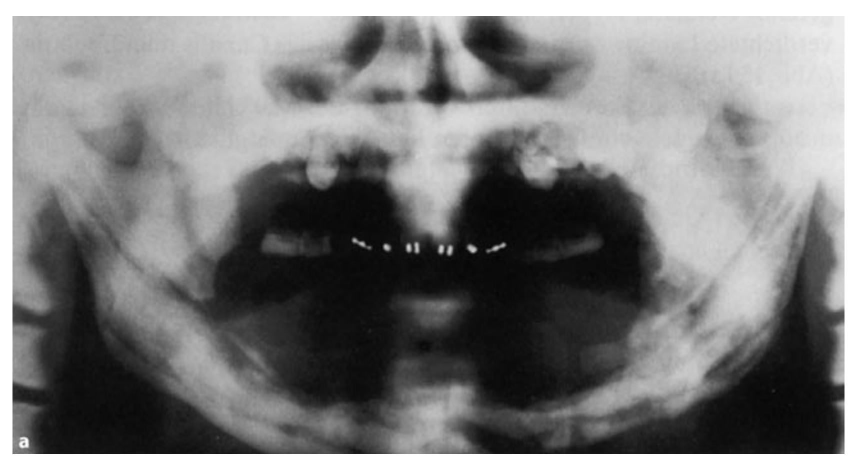
The jawbone in osteopetrosis cases shows massive sclerosis (Fig. 2.32). Because of the disturbed physiology

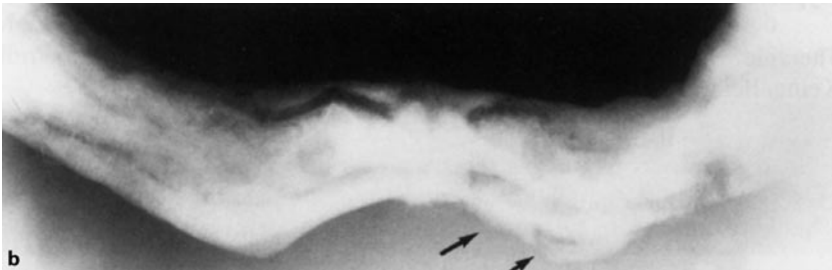
Table 2.20 Differential diagnosis of acute and secondary chronic osteomyelitis of the jaws

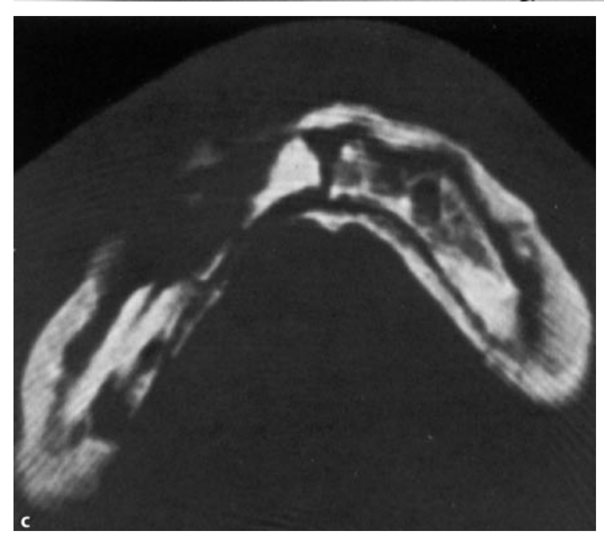
Differential diagnosis of acute and secondary chronic osteomyelitis of the jaws
Acute and early-stage secondary chronic osteomyelitis (predominant osteolysis)
– Primary bone tumors
– Bone metastasis
– Primary intraosseous or invasive growing squamous cell carcinoma
– Early osteoradionecrosis
– Eosinophilic granuloma
– Plasmocytoma
– Demineralized bone in dialysis patients
Advanced-stage secondary chronic osteomyelitis (osteolysis and sclerosis)
– Primary bone tumors
– Bone metastasis
– Primary intraosseous or invasive growing squamous cell carcinoma
– Osteoradionecrosis
– Osteochemonecrosis (bisphosphonate induced)
– Plasmocytoma
– Demineralized bone in dialysis patients
– Tendoperiostitis
– Primary chronic osteomyelitis

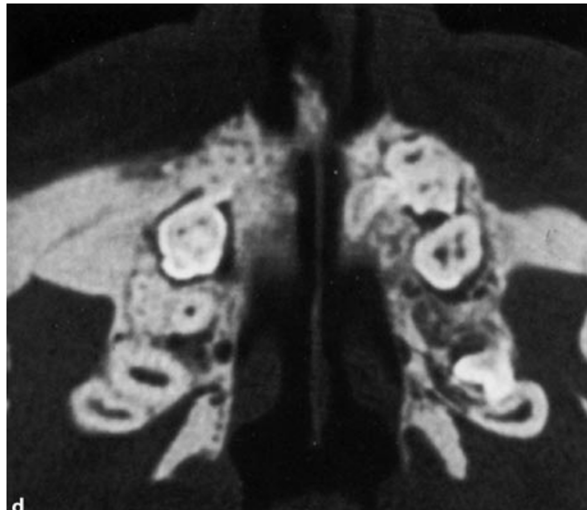
Table 2.21 Differential diagnosis of primary chronic osteomyelitis of the jaws

Differential diagnosis of primary chronic osteomyelitis of the jaws
• Fibrous osseous dyplasia (FOD/Jaffé-Lichtenstein)
• Periapical cemental dysplasia
• Enostosis (compact island), bone scar
• Ossifying fibroma, osteoma, osteochondroa
• Osteosarcoma
• Tendoperiostitis
• Paget's disease (deforming ostitis)
• Osteopetrosis (Albers–Schonberg disease)









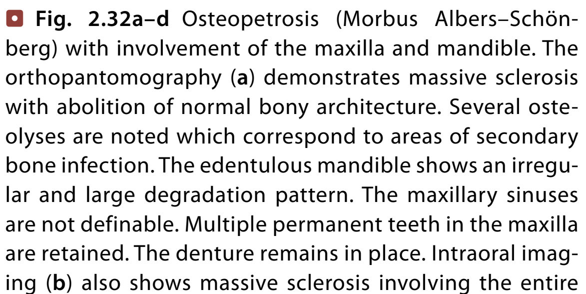


Fig. 2.32a–d Osteopetrosis (Morbus Albers–Schönberg) with involvement of the maxilla and mandible. The orthopantomography (**a**) demonstrates massive sclerosis with abolition of normal bony architecture. Several osteolyses are noted which correspond to areas of secondary bone infection. The edentulous mandible shows an irregular and large degradation pattern. The maxillary sinuses are not definable. Multiple permanent teeth in the maxilla are retained. The denture remains in place. Intraoral imaging (**b**) also shows massive sclerosis involving the entire mandible, streaked by bands of osteolysis (*arrows*). The corresponding axial CT scans of the mandible (**c**) and maxilla (**d**) demonstrate a clearer picture of the osteosclerosis and osteolytic pattern. The osteolytic pattern surrounds the body of the mandible and is demarcated by a sclerotic band on the outer surface corresponding to a strong periosteal reaction (**c**). In the maxilla a sclerosis and thickening of the bone is predominant with complete obliteration of the maxillary sinus. Multiple retained permanent teeth are shown (From Bayer et al. 1987)

of the bone with insufficient function of the osteoclast cells, the osteopetrotic bone cannot be resorbed adequately and sclerosis increases with time, jeopardizing bone perfusion. Secondary infection of the bone is therefore commonly observed in these patients, and the clinical picture resembles primary or secondary chronic osteomyelitis with predominant sclerosis. Because bone physiology is generally disturbed, both jaws may be completely affected by the pathology, contrary to primary chronic osteomyelitis which generally just affects the mandible.

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3 Diagnostic Imaging – Conventional Radiology, Computed Tomography and Magnetic Resonance Imaging

Bernhard Schuknecht

Contents

3.1 Summary

Imaging is a crucial diagnostic tool in the assessment of acute and chronic osteomyelitis of the jaws. Before any cross-sectional imaging modality is applied, the orthopanoramic view is the first image to assess the status of dentition, recognize direct radiographic signs of osteomyelitis, narrow the differential diagnosis, and depict potential predisposing conditions such as a fracture or systemic bone disease. The orthopanoramic view is furthermore the first-line image when follow-up examinations are performed.

In acute osteomyelitis the higher sensitivity of magnetic resonance imaging (MRI), with respect to detection of intramedullary inflammation, advocates its use as the imaging modality of choice to confirm the diagnosis and provide an estimate of the intraosseous extent and soft tissue involvement.

In case surgical treatment is planned, high-resolution computed tomography (CT) is required to specify the degree of cortical destruction, delineate the presence of sequestra, and to define the extent of osseous removal required.

In chronic osteomyelitis the higher sensitivity of CT with respect to detection of sequester and sclerotic bone changes renders CT the examination of choice to distinguish the usually more uniform and extensive primary chronic osteomyelitis from the more localized type of secondary chronic osteomyelitis. Magnetic resonance imaging is superior to detect periosteal inflammation and soft tissue involvement and thus aids in determining the persistence or recurrence of infection. Following surgery, CT is preferred as follow-up examination for a

period of 6 months to distinguish postoperative and reparative changes from recurrent or persistent infection.

Complimentary information is gained in particular situations by a combination of imaging modalities adapted to the individual patient's course of disease and the panoramic view findings.

An overview of the diagnostic imaging pathway in patients with suspected osteomyelitis of the jaws is given in Fig. 3.1.

3.2 Role of Imaging

Radiology plays an essential role in the imaging work-up of infectious and inflammatory conditions affecting the bimaxillary skeleton. Based on the number of radiological examinations positive for osteomyelitis of the jaws, an annual incidence of 1:80,000 persons is estimated for Switzerland.

Osteomyelitis is the most serious manifestation of an infection of the facial skeleton. Contrary to the mandible, the maxilla is only rarely affected. Osteomyelitis of the upper jaw accounts for only 1–6% of patients (Schuknecht and Valavanis 2003; Baltensperger 2003).

In view of potential severe functional and aesthetic consequences, early diagnosis of osteomyelitis is mandatory in order to establish appropriate treatment. "Adequate" imaging is aimed at precise assessment of the bone and the soft tissue for inflammatory changes to confirm the diagnosis early, delineate the extent of disease precisely, and recognize potential complications or a tendency toward chronicity. A rational use of the imaging modalities is of utmost importance, as is to avoid unnecessary radiation.

In order to confirm and assess osteomyelitis of the jaws, a spectrum of radiological techniques from which to choose is available. Conventional radiographs serve as first-line examination. Computed tomography (CT) and MRI are well-established high-resolution cross-sectional imaging techniques which provide precise morphological information regarding bone and soft tissue involvement.

With scintigraphy a sensitive technique is available – limited only by low spatial resolution and specificity. Fusion positron emission tomography–CT (PET–CT) offers a combined technique using both the advantages of CT imaging and labelled radionucleotides to gather information on anatomical structure and metabolic activity of the examined region.

A short comparison of bone-scan techniques to standard conventional radiological imaging, CT and MRI is given herein. The technical aspects, benefits and disadvantages of scintigraphy and PET in the diagnosis of jawbone osteomyelitis are discussed more extensively later in Chaps. 4 and 5. Cone-beam tomography is a relatively new technique that uses low radiation dose to display bone with a high spatial, but limited contrast, resolution.

Adequate and rational application of imaging is directed toward the following goals:

- Confirm the presence of an infection or inflammation with respect to involvement of the lower or upper jaw
- Recognize a local source of infection and/or a predisposing osseous condition

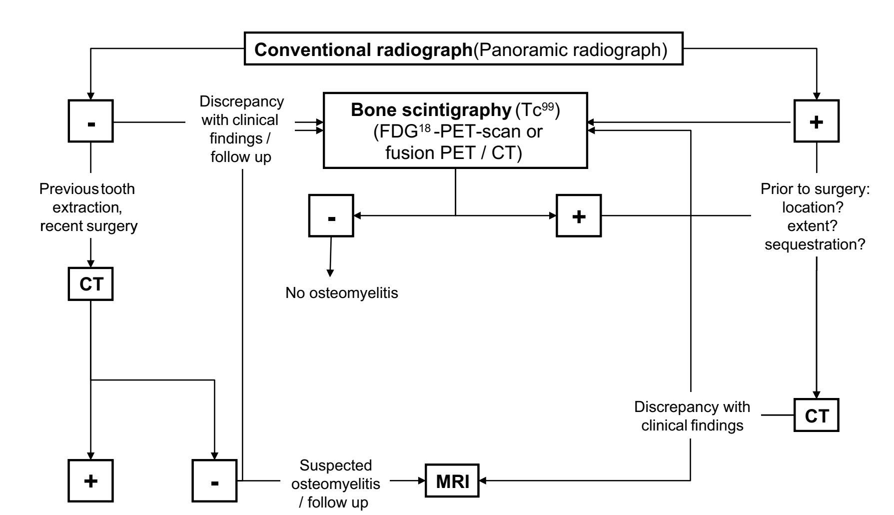


Fig. 3.1 Diagnostic imaging pathway in patients with suspected osteomyelitis of the jaws

- Delineate the location and extent of osseous infection and potential concomitant soft tissue involvement
- Distinguish osteomyelitis from lesions that may mimic infection/inflammation of the jaws
- Identify participation of the jaws as part of a syndrome or a multifocal inflammatory process
- Delineate potential complications during the natural course or following treatment

3.3 Imaging Techniques

3.3.1 Conventional Radiology

Among conventional radiographs, the orthopanoramic view is of primary importance as it depicts the status of the dentition, displays the osseous confines and internal osseous structure of the jaws, and is the adequate basis for a follow-up examination. The orthopanoramic view may be occasionally supplemented by intraoral radiographs. Both techniques have the advantage of being at the disposition of the dentist or maxillo-facial surgeon. Even though called "conventional," the radiographs in the majority of institutes are acquired in a digital format as well. Radiation dose for the panoramic view is lowest with 0.3 mSv.

Additional radiographs may be required to focus on certain anatomical areas: The mandibular oblique view is occasionally justified to provide a better projection of one side of the mandibular body, the occlusal view to depict the symphysis and maxilla area. The posteroanterior view of the mandible (Clementschitsch) is suited to delineate the mandibular condyles and Waters view to assess the maxillary sinuses.

3.3.2 Computed Tomography and Magnetic Resonance Imaging

Computed tomography and MRI have gained considerable importance over the past 20 years as they provide high-resolution morphological information with respect to compact and cancellous bone and soft tissue. These so-called cross-sectional imaging techniques avoid overprojection of structures in the second dimension and thus differ from conventional radiographs, which are referred to as "projectional techniques."

Computed tomography uses fan-beam collimated radiation, which is applied with continuous motion while at the same time the scanning region is moved. The resultant images are reconstructed from a spiral CT data set. Images thus allow assessing the oro-vestibular dimension as well as the baso-alveolar and the mesio-distal extent of the mandible by reconstruction of axial, coronal and sagittal planes, usually from one data set acquired in the axial plane. Computed tomography is particularly suited to depict cortical bone involvement as well as delineate erosion of the confines of the mandibular canal, the mental foramen and the superior alveolar process and tuber maxillae. Computed tomography serves as gold standard to display calcified periosteal reactions. Compared with radiographs, the sensitivity is considerably higher in detecting the early changes of acute osteomyelitis. New spiral 64-row CT scanners allow high-resolution imaging of bone with a volume element size (voxel size) as small as 0.3 mm^3. Reconstructions in multiple planes enable precise delineation of altered bone structure and morphology. In addition to bony changes, CT is able to assess concomitant soft tissue inflammation. Higher dosage is therefore required, which is in the range of 0.5–3 mSv. Intravenous injection of iodine as contrast agent is obligatory to assess alterations of the blood tissue barrier. This refers to recognition of an abscess or phlegmonous infiltration affecting the vestibulum oris and/or submandibular and submental space. Rare sites of abscess locations are perimandibular along the ascending ramus or the parapharngeal space. Limitations for CT are artefacts originating from amalgam and other alloy dental fillings which may degrade image quality to such a degree that the soft tissue information is lost within the particular plane. Despite these artefacts, the bony information is usually preserved.

Magnetic resonance imaging is a technique that is not based on radiation but on proton relaxation within a static high magnetic field. T1 relaxation is based on longitudinal relaxation and displays fluid as hypointense (dark) signal. T1 images provide the basis for assessment of contrast enhancement. Unlike CT, MRI uses gadolinium (Gd) as contrast agent. Gadolinium has the propensity to shorten the T1 relaxation time, which is displayed as high signal (bright) within tissue, when the blood tissue barrier is disturbed. Contrast enhancement as a non-specific process occurs in infection, inflammation, tumour or trauma. Contrast enhancement indicates the location and extent of soft tissue and cancellous bone involvement.

T2 effects are based on transverse relaxation and are indicated by increased hyperintense (bright) signal within fluid and oedema and are not combined with contrast agent. Technical refinements have led to

considerable modifications of the T1- and T2-weighted MRI "sequences" with a particular sensitivity to recognize tissue changes. Contrary to CT, each sequence is performed separately within a single plane by additional measurements of proton relaxivity. The examination is therefore considerably more time-consuming.

Magnetic resonance imaging has developed as a sensitive imaging technique to recognize early medullary bone involvement. The availability of mobile protons within medullary fat accounts for the high sensitivity of MRI for any process that extends over the confines of cortical bone to affect cancellous bone. Inflammation is accompanied by an increase in water content with abundant mobile protons indicated by bright signal on T2 images and low signal on T1 and contrast enhancement. The sensitivity of MRI therefore surpasses CT with respect to cancellous bone extension, as well as recognition of non-calcified periosteal reactions.

The firm integration of calcium protons within cortical bone, on the other hand, renders cortical bone almost invisible unless it is destroyed by inflammation or tumours. The sensitivity to detect cortical-plate changes by MRI, in general, is lower than on CT images. Concomitant participation of the muscles of mastication is more readily recognized by MRI than by CT. The advantage of higher sensitivity relegates MR examinations to those patients in whom a normal or near-normal orthopanoramic radiograph contrasts with severe symptoms such as trismus, reduced mouth opening or inferior alveolar nerve hypesthesia. The poor ability of MRI to depict cortical bone – contrary to cancellous – bone limits the value of MRI within the maxilla and as a means for surgical treatment planning.

3.3.3 Cone Beam Volume Tomography

Cone beam volume tomography is a new technique designed for dental and maxillofacial examinations. The technology – even though frequently also called CT or cone-beam computed tomography (CBCT) – harbours fundamental differences from CT. A cone-shaped radiation beam is rotated once around the region of interest. Cone-beam tomography does not provide soft tissue information. Lower tube dosage is applied, which significantly reduces radiation dose. Effective radiation dose is about 0.3 mSv. Consequently, the susceptibility to artefacts arising from dental fillings is markedly lower. Acquisition of a 3D volume data set using a cylinder of 40×40 mm and 60×60 mm (3D Accuitomo; J. Morita Corp., Osaka, Japan) enables higher spatial resolution with a voxel size of 0.125 mm^3 compared with 0.3 mm^3 as the lower limit for CT. An alternative cone-beam technique (NewTom QR, AFP Imaging, Elmsford, N.Y.) uses a 100- to 210-mm focused cone-beam projected to a square two-dimensional array of detectors. From the raw data set a reconstruction algorithm enables reconstruction of slices with a spatial resolution of 0.16–0.36 mm. Limitations of the cone-beam technology consist of the inability to depict soft tissue, the long data acquisition time of 18–36 s (to 75 s), and the low contrast resolution within compact bone. Volume tomography has therefore gained importance in issues such as implantology, evaluation of impacted third molars and the assessment of cysts. The ability to detect osteomyelitis based on irregular radiolucencies and osteosclerotic changes has recently been described (Schulze et al. 2006). With the upcoming popularity and the rapid advances in cone-beam technology this imaging modality might show growing intrest in the future for this indication.

3.4 Classification

As is well known by those who are involved in the diagnosis and treatment of patients, osteomyelitis of the jawbones may present a clinically wide variety, depending on the location and acuity of the disease, previous treatment and concomitant diseases, the age of the patient and the potential aetiology.

Prior to the availability of high-resolution CT or MRI, limited awareness of the disease, probably restrictive application of conventional X-rays, and limited sensitivity of conventional radiographs accounted for the fact that acute osteomyelitis was only rarely recognized and diagnosed. Both CT and MRI have significantly contributed to increased recognition of the acute manifestations of this disease (Schuknecht et al. 1997).

Historically, the focus on chronic osteomyelitis has been revealed by designations such as "diffuse sclerosing osteomyelitis", "osteomyelitis sicca" or "nonsuppurative osteomyelitis", "periostitis ossificans (Garré)", and "chronic recurrent multifocal osteomyelitis." A confounding nomenclature has arisen that reflects various histological or radiographic aspects of chronic osteomyelitis rather than truly different clinical manifestations. As the acute stage hardly came to attention, diagnosis and treatment primarily dealt with the chronic manifestations of osteomyelitis. The heterogeneity of chronic osteomyelitis with respect to clinical and radiographic appearance has been confirmed by previous reports

(Schuknecht et al. 1997; Baltensperger 2003; Baltensperger et al. 2004) and analysed in order to establish a clear classification based on these criteria (Baltensperger 2003; Baltensperger et al. 2004).

The necessity of a classification was stated by Calhoun and coworkers (1988) for reasons that "initial treatment planning can be safely and successfully based on the stage of the disease." Decortication as a treatment of osteomyelitis was reported by Hjorting-Hansen (1970) and supplemented by Obwegeser and Sailer (1978) and Sailer (1991) by partial resection and immediate reconstruction. Substantial changes in the recognition and treatment of mandibular osteomyelitis fostered the necessity for a classification in order to adequately apply and direct surgical treatment (Sailer 1991).

Marx (1991) and Mercuri (1991) defined acute and chronic osteomyelitis by the duration of symptoms after onset of disease. These definitions have gained wide acceptance in the medical and dental communities and were also incorporated in the so-called Zurich Classification of Osteomyelitis of the Jaws, which is advocated in this book. This classification is extensively addressed in Chap. 2.

Based on clinical and radiological criteria, osteomyelitis can be staged into two principal categories: acute osteomyelitis and chronic osteomyelitis. Acute osteomyelitis covers a time frame of 4 weeks after onset of disease (Marx 1991) and (Mercuri 1991). The frequently preventive application of antibiotics, improved dental health and changes in diagnostic techniques has probably led to a change in incidence and character of acute osteomyelitis (Hardt and Grau 1987). In addition to the designation "acute" osteomyelitis, the term "subacute" osteomyelitis is infrequently used (Schuknecht et al. 1997; Schuknecht and Valavanis 2003). It refers to a transitional stage within the time frame of acute osteomyelitis and corresponds to advanced acute osteomyelitis in the third and fourth weeks after onset of disease (Schuknecht et al. 1997).

After the arbitrarily set time limit of 4 weeks, acute osteomyelitis is followed by "chronic" osteomyelitis (Marx 1991). The duration of osteomyelitis to reach the chronic stage is therefore already – when first recognized – at least 1 month.

The term "secondary chronic osteomyelitis" is applied when the inflammatory process is the continuation of an acute episode. The designation "secondary chronic osteomyelitis," however, is also appropriate when the acute stage passed undiagnosed but, at least in retrospect, can be related to an event or symptoms within the preceding 4-week period.

The term "primary chronic osteomyelitis" implies that the patient has never undergone an appreciable acute phase and lacks a definitive inciting insult. Primary chronic osteomyelitis of the jaw is a rare, nonsuppurative, chronic inflammatory disease of unknown aetiology. It tends to arise de novo and follows an insidious course. An affiliation with SAPHO syndrome and chronic recurrent multifocal osteomyelitis (CRMO) is found in some patients (Baltensperger et al. 2004). Both manifestations are considered types of seronegative spondyloarthropathies.

Radiological imaging, such as clinical appearance and course of the disease, provides an important criterion to substantiate the aforementioned classification and is therefore considered as a primary classification criterion in the Zurich Classification of Jawbone Osteomyelitis (Schuknecht et al.1997; Schuknecht and Valavanis 2003; Baltensperger 2003; Baltensperger et al. 2004).

3.5 Acute Osteomyelitis: Conventional Radiology

The panoramic view is the first examination in a patient clinically suspected of having developed osteomyelitis of the jaw. Depiction of the status of the dentition and of the bone structure is readily provided by the OPT. Following a dental procedure, a tooth extraction in the molar region in particular, osteomyelitis may develop either due to persistence of a preexisting focus or due to de novo infection of the tooth socket. Comparison of the recent panoramic view with previously performed radiographs facilitates recognition and distinction of an incipient new infection or persistence and reactivation of a previous process. Additional radiographs are rarely required.

Radiographs may fail to reveal any change for 4–8 days (Worth and Stoneman 1977). Until the inflammation has resulted in sufficient dissolution of bony trabeculae, conventional radiographs are interpreted as normal (Fig. 3.2a).

Bone resorption due to hyperaemia and osteoclastic activity requires 30–50% focal reduction of bone mineral content in order to be recognized by radiographs (Worth and Stoneman 1977); therefore, it is not uncommon for plain films to be interpreted as normal up to 2 weeks or occasionally 3 weeks after the onset of symptoms (Davies and Carr 1990). In a study comparing conventional radiographs and CT (Schuknecht et al. 1997), plain films were interpreted normal in 3 of 4 patients

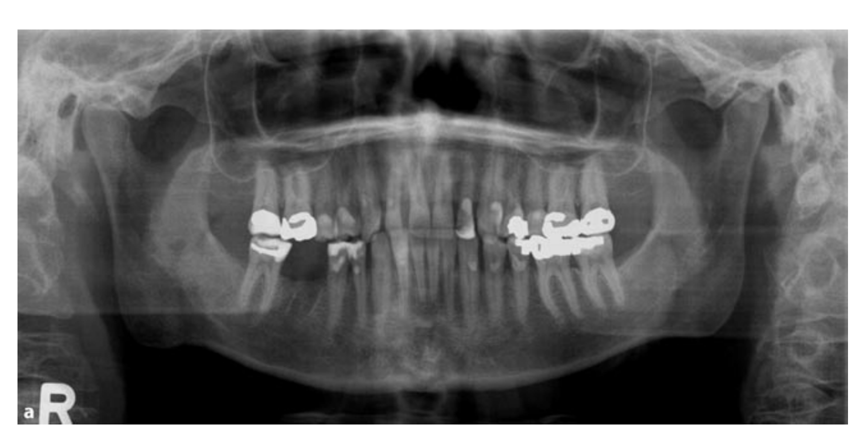


Fig. 3.2a–e Acute osteomyelitis of the right mandible: a 36-year-old man 2 weeks following extraction 46. Clinical symptoms at this point were progressive pain, recent onset of hypesthesia, and swelling along right mandible. The panoramic view (**a**) is unremarkable with normal-appearing empty tooth socket following removal of 46. **b–e** *see next page*

(75%) within the first 2 weeks. In only 3 of 8 patients (37.5%) were radiographs proved pathological within a time frame of 4 weeks after initiation of symptoms; however, within the fourth week radiographs had definitively turned pathological (Schuknecht et al. 1997).

An overview of the signs in conventional radiology in acute osteomyelitis of the jaws is given in Table 3.1.

The first sign of osteomyelitis is loss of the trabecular structure of bone resulting in a focal area of radiolucency. The area of osteolysis is commonly related to an empty tooth socket or a diseased tooth. Initial radiographic indicators may be a widened periodontal ligament space or a defect of the lamina dura. Destruction of bone initially proceeds within cancellous bone. The cortical plate is secondarily involved by progressive bone resorption and increasing pressure exerted by the inflammation. Additional early signs are erosion of the endosteal contour of the basal mandibular cortical bone or in the upper jaw effacement of the contour of the alveolar maxillary recess.

Plain films, even though initially frequently negative for osteomyelitis, are able to display a potential odontogenic source of infection (Fig. 3.2a). Lesions like apical periodontitis, periodontal disease or deep caries may provide a pathway for the spread of infection. In some patients, however, a parodontal or dental inflammatory focus may be absent.

Trauma follows odontogenic causes in frequency. Fractures affecting the tooth-baring portion of the mandibular body account for a major part of infections (Baltensperger 2003). Radiographic distinction of the natural course of the fracture with increasing lucency along the fracture line from an infection induced area of bone resorption in the early stage is hardly possible. Radiolucency along screws and plates are indicative of early infection. A high degree of clinical suspicion is therefore required leading to early CT (particularly with osteosynthesis) or MRI.

Within the third and fourth weeks radiographs tend to become mostly pathological. Findings consist of usually ill-defined areas of radiolucency, sequestra, calcified periosteal reactions and occasionally fistulae. In this advanced stage of acute osteomyelitis sequester may add to the radiological findings. Based on conventional images, the occurrence of sequester is considered rare within the first 4 weeks and more typically is referred to the chronic stage (Vargas et al. 1984; Kaneda et al.1995). In one study sequestra were missed on plain films in one-third of patients within the advanced stage of acute osteomyelitis (Schuknecht et al.1997). A pathological fracture adjacent to an area of ill-defined radiolucency and radiopacity may add to the likelihood of the presence of a sequester (Fig. 3.3a).

The low incidence of sequestra on conventional radiographs is related to the fact that the islands of bone that maintain radiopacity are difficult to recognize within an area of osteolysis or along fracture lines (Fig. 3.4).

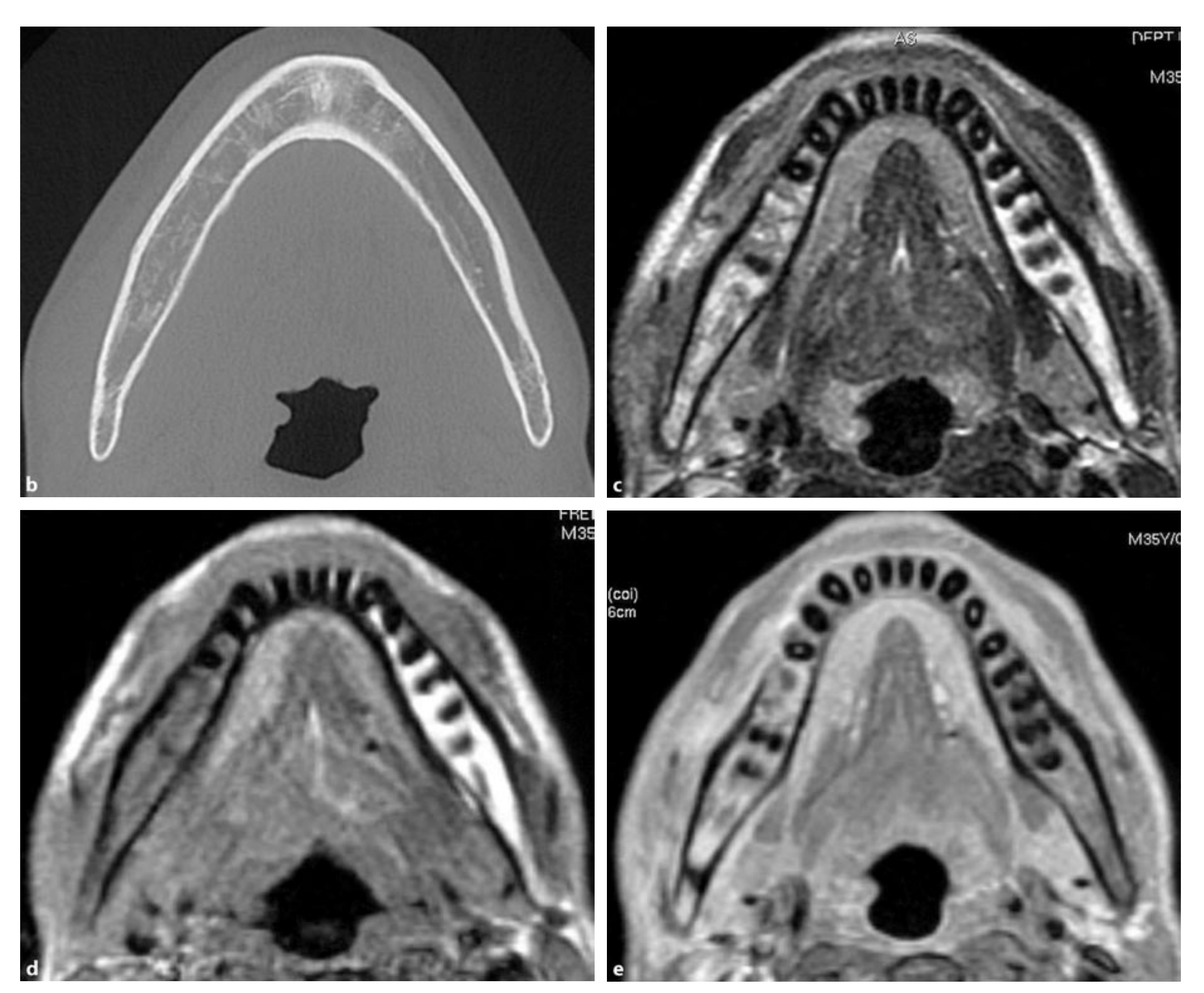


Fig. 3.2a–e (*continued*) Axial high-resolution bone window CT image (**b**) depicts mild right-sided soft tissue swelling, demineralization and reduction of cancellous bone trabeculae, slight demineralization of buccal and lingual cortical plate (in comparison with contralateral side) and linear cortical bone interruption on lingual side. Axial T2 MR image performed the same day (**c**) displays heterogeneous signal within cancellous bone with low signal components indicating cellular infiltration, loss of contour and signal change of the right masseter muscle. Non-contrast T1 MR image (**d**) reveals replacement of marrow fat by hypointense (*dark*) signal, which changes into hyperintense (*bright*) signal following contrast application on gadolinium (Gd)-enhanced, fat-suppressed T1 MR image (**e**). There is linear bright signal along the buccal and lingual compact bone corresponding to periosteal inflammation and involvement of masseter muscle

Table 3.1 Conventional radiological signs in acute osteomyelitis of the jaws

Conventional radiological signs in acute osteomyelitis of the jaws (1–4 weeks after onset of disease)	
Acute osteomyelitis (1–2 weeks) • Increased radiolucency • Loss of trabecular structure • Loss of contour of mandibular canal • Pseudo-widening of mental foramen and mandibular canal • Erosion of cortical bone	Acute osteomyelitis (3–4 weeks) • Radiolucent line around cortical bone with increased radiopacity indicating sequester formation • Linear irregular radiolucencies within (basilar) cortical related to fistulae • Calcified periosteal reaction • Minor areas of sclerosis interspersed with a zone of increased radiolucency • Fracture as potential complication

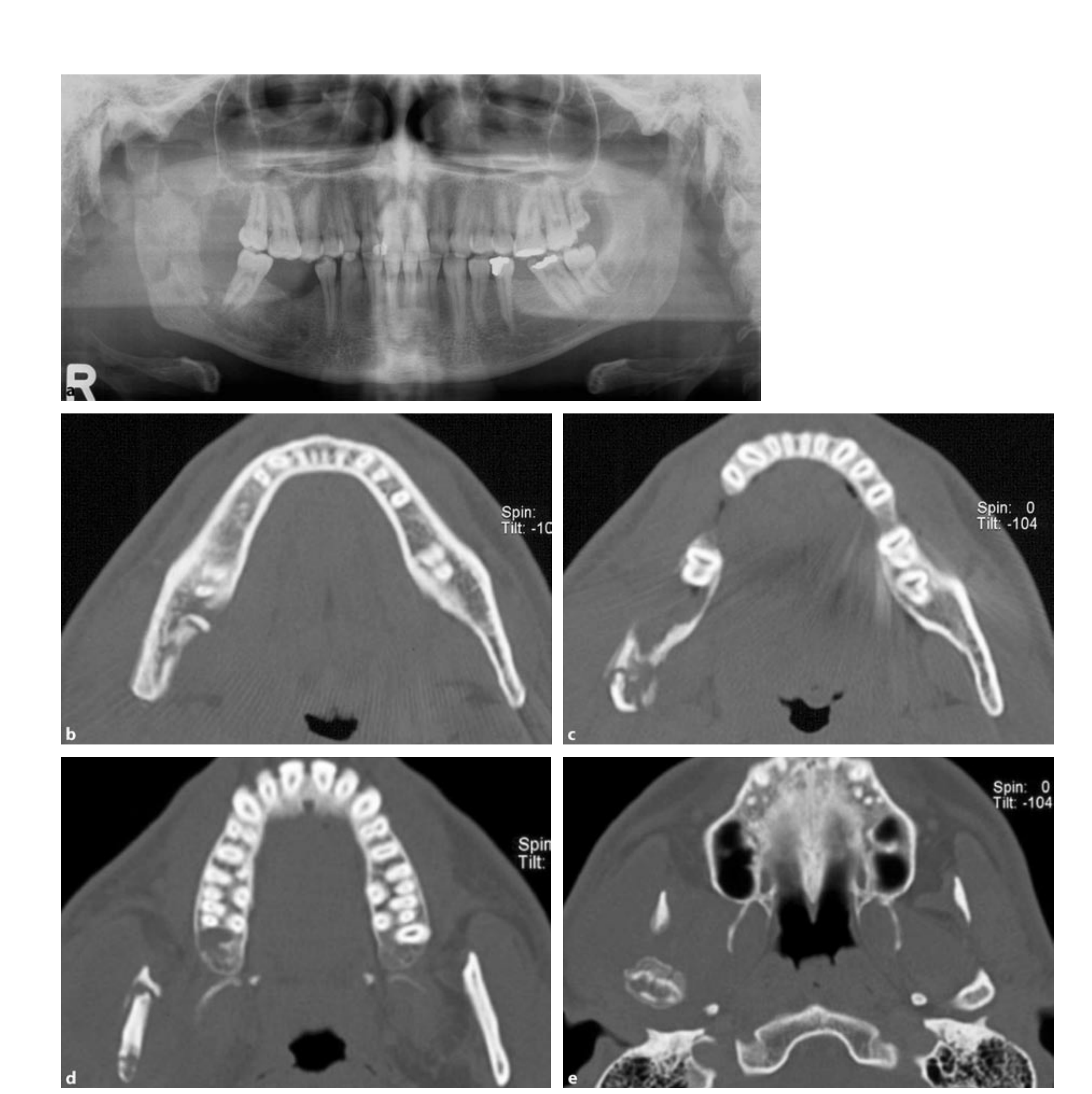


Fig. 3.3a–g Advanced-stage acute osteomyelitis with beginning transition into secondary chronic osteomyelitis: a 24-year-old man 5 weeks after surgical removal of 48 and extraction of 18 presents with 3.5 weeks progressive pain, marked swelling, hypesthesia and reduced mouth opening. The panoramic view (**a**) depicts linear areas of radiolucency affecting retromolar area, lower ramus and level of semilunar incisure with deconfiguration of mandibular column and condyle. Suspicion of sequestration of coronoid process with pathological fracture, loss of internal oblique line and mild elevated opacity of bone with effacement of mandibular canal are additional findings. Axial high-resolution bone-window CT images from basilar portion of mandible (**b**), retromolar area (**c**), level of semilunar incisure (**d**) and condyle (**e**) display thickening and mild sclerosis of mandibular angle adjacent to buccal surgical defect. **f,g** *see next page*



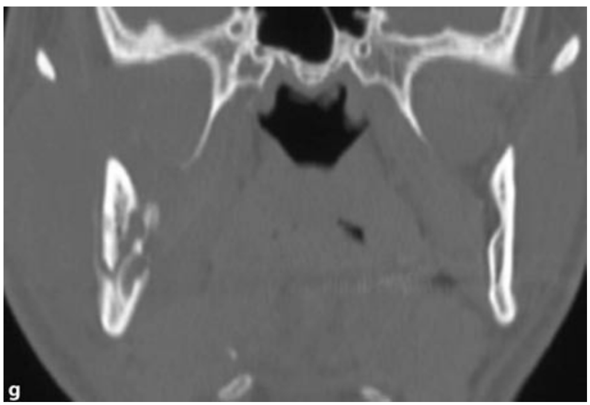


Fig. 3.3a–g (*continued*) The dorsal part of the mandibular angle has undergone sequestration as well as part of the coronoid process, as is also shown by coronal high-resolution bone-window CT images (**f,g**). Note linear periosteal reaction along buccal side of ramus partially covering sequestered coronoid process and encircling demineralized condyle. Masseter muscle is markedly thickened

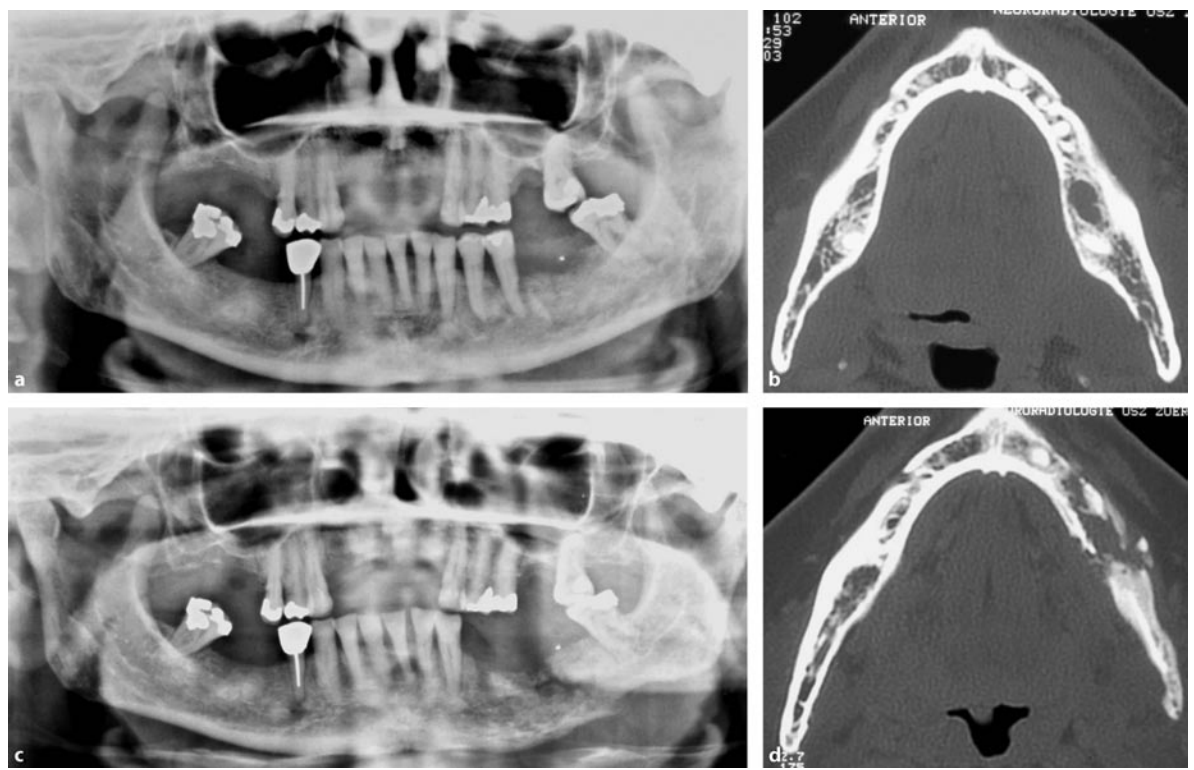


Fig. 3.4a–d Acute osteomyelitis and transition into secondary chronic osteomyelitis with sequestration and pathological fracture: a 63-year-old woman 2.5 weeks after extraction of carious left lower molar with new onset of left mandibular swelling. Panoramic view (**a**) does not provide any clue to the presence of osteomyelitis. The axial high-resolution bone-window CT image (**b**) displays slight thinning, demineralization and endosteal resorption of lingual cortical plate. Three months later (during second course of antibiotic therapy), the patient presents with sudden onset of pain and marked malocclusion. The panoramic view (**c**) discloses an irregular osteolytic area, a fracture traversing the remaining basilar bone and suspicion of multiple sequester with some degree of bone radiopacity. The presence of two buccal sequesters, partial cortical plate resorption, irregular calcified periosteal apposition and cancellous bone osteolysis and distal sclerosis is shown by the axial high-resolution bone-window CT image (**d**). Due to the sectional character, the individual CT slice is inferior to conventional X-ray images in showing the fracture line (From Schuknecht et al. 1997)

A particular type of sequester is the "involucrum." The definition demands the presence of a sequester covered by bone. Sequestra and periosteal bone formation serve as radiological "indicators" in the advanced stage of acute osteomyelitis and thus play a significant role in arriving at the diagnosis.

Periosteal reactions may affect all nonalveolar borders of the mandible. A periosteal reaction related to the maxilla is exceedingly rare. On conventional radiographs periosteal reactions consist of a predominantly single layered, linear radiopacity separated by a lucent line from the mandibular cortical bone. Related to the ease with which the periosteum is stripped from the mandibular cortex and the increased osteogenic potential, the periosteal reaction is more pronounced in young patients. When occurring along the inferior aspect of the mandible periosteal new bone formation is best visualized on lateral oblique or panoramic radiographs.

The more common location along the body of the mandible tends to escape detection. Although posteroanterior mandibular and occlusal views produce few positive results, a series of ten patients was described in which periosteal calcification was evident solely on these projections (Nortje et al. 1988). When comparing conventional films and CT, a higher incidence of periosteal reactions on CT is noted (Ida et al. 1997; Schuknecht et al 1997).

This holds also true for osseous fistulae as well. Only one of the three fistulae that were detected by CT could on retrospect be identified on conventional radiographs (Schuknecht et al. 1997).

Consequently, with the exception of the panoramic view most of the plain films have been abandoned in favour of early application of a CT or MRI examination.

3.6 Scintigraphy

Markedly increased bone turnover activity is indicated by scintigraphy and has been reported as an early sign in acute osteomyelitis (Rohlin 1993; Köhnlein et al. 1997). Increased activity due to hyperaemia is detected as early as 2–3 days after the onset of symptoms (Reinert et al. 1995). The degree of uptake was reported as higher when plain films showed permeative bone destruction and areas of osteolysis compared with the moth-eaten or sclerotic appearance that prevails in chronic osteomyelitis (Rohlin 1993). With histology as reference, the sensitivity in the acute phase is postulated to be close to 100% and false-negative results are attributed to the fact that the examination has been performed too early (Köhnlein et al. 1997).

Drawbacks of scintigraphy in acute osteomyelitis are related to fact that distinction between soft tissue inflammation and bone involvement is limited (Tsuchimochi et al. 1991; Rohlin 1993). As a preoperative examination scintigraphy is not sufficient to determine the extent of mandibular osteomyelitis. It has to be complemented by an additional CT examination to provide the detailed osseous information required (Schuknecht et al. 1997; Heggie 2000). As a follow-up examination simultaneous indium-111 WBC/Tc-99m-MDP bone SPECT scintigraphy has been found to revert back to normal after successful treatment much sooner than CT (Weber et al. 1995)

A more detailed description of scintigraphy and its role in imaging diagnosis of acute osteomyelitis of the jaws is given in Chap. 4.

3.7 Computed Tomography

3.7.1 Examination Technique

A spiral, cranio-caudad acquisition with thin collimation (0.5–1.0 mm) is obtained covering the maxilla and the mandibula to the hyoid bone with the patient in a supine position. Acquisition of a second (coronal plane) with the patient in a prone position is no longer recommended. Proper, well-aligned positioning of the head facilitates reconstruction of the axially acquired image data set into axial oblique and coronal planes. The reconstructions are performed with a slice thickness of 2 mm, the inclination is angulated anteroinferiorly parallel to the mandibular body for the axial plane, along the mandibular ramus for the coronal plane. Curved or sagittal oblique reconstructions along the mandibular body provide information similar to an orthopanoramic radiograph. Documentation of CT images with a bone-window algorithm images is with window/level (W/L) settings of 3200/700.

Recognition and differentiation of facial and masticator space inflammation requires intravenous application of iodine-containing contrast material which is performed with 100 ml at a flow rate of 2 ml/s. The soft tissue images which are reconstructed from the axial data set are displayed as coronal and axial oblique 3-mm slices with a window/level setting of W/L 300/100.

3.7.2 Findings

Computed tomography has been increasingly used to evaluate the presence and extent of mandibular osteomyelitis including accompanying soft tissue inflammation (Osborn et al. 1982; van Merkesteyn et al. 1988; Felsberg et al. 1990; Kanemoto et al. 1992; Ohlms et al. 1993; Yoshiura et al. 1994; Schuknecht et al. 1997; Schuknecht and Valavanis 2003; Ida et al. 2005). The capability of CT to combine osseous and soft tissue information with high spatial resolution was recognized early (Osborne et al. 1982); however, only after a latency has CT been used in patients suspected of harbouring osteomyelitis of the mandible (van Merkesteyn et 1988; Felsberg et al. 1990; Kanemoto et al. 1992; Ohlms et al 1993; Yoshiura et al. 1994; Kaneda et al 1995; Schuknecht et al. 1997; Ida et al. 2005).

Despite the ability of CT to provide a more definitive picture of bony involvement compared with conventional radiographs in the acute stage, a limited number of patient series has been investigated during the first 4 weeks of inflammation only (Yoshiura et al. 1994; Kaneda et al. 1995; Weber et al. 1995; Schuknecht et al. 1997).

An overview of the signs in CT in acute osteomyelitis of the jaws is given in Table 3.2.

The CT findings in the acute stage of osteomyelitis consist of an area of osteolysis that initially is confined to cancellous bone (Fig. 3.2b). The cortical bone may be affected resulting in demineralization and focal decreased density. Minor perforations to reach the subperiosteal space are additional signs (Figs. 3.2b, 3.5b). Extension typically proceeds within the medullary cavity. Cancellous bone infection may extend as far as the mandibular condyle with only minor cortical bone osteolysis (Fig. 3.5c). Intramedullary extension tends to pass along the mandibular canal to reach the mental foramen (Fig. 3.6).

In addition to cancellous bone extension, infection tends to cause erosion and thinning of the endosteal and/or periosteal cortical plate. The CT depicts loss of cancellous bone trabeculae, loss of contour of the mandibular canal, and a widened mental foramen. Occasionally preexisting osteoporosis leading to reduced cancellous bone density may render recognition of the initial phase of acute osteomyelitis difficult by CT as well.

A different appearance of acute osteomyelitis is related to preexisting chronic periapical or parodontal infection. Sclerosis of the adjacent cancellous bone may wall off the acute infection and impede intramedullary extension. Consequently, early localized transcortical perforation of the intramedullary abscess may be observed (Fig. 3.7).

Higher sensitivity of CT in comparison with plain radiographs has been reported in 2 of 4 patients investigated during the acute stage (Kaneda et al. 1995). In the other two patients CT was false negative as well. In another 2 patients (Weber et al. 1995) CT was positive for mandibular osteomyelitis in 1 patient, while it demonstrated soft tissue oedema but missed the bone abnormality in the other case.

In 4 patients investigated during the first 2 weeks of osteomyelitis, conventional X-rays provided the diagnosis in only 1 of 4 patients (25%) (Schuknecht et al. 1997), while in a second group of 4 patients examined during the subacute phase (third and fourth weeks), positive X-ray findings were present in 3 of 4 patients (75%). On comparison, CT showed the area of osteolysis to be one molar or premolar region larger than on conventional radiographs.

The mandibular body is the most frequent site with 75–83% of primary locations (Ida et al. 1997; Schuknecht et al.1997; Baltensperger 2003). The angle of the mandible is concomitantly involved in about half of these patients (van Merkesteyn et al. 1988; Koorbusch et al. 1992; Ida et al.1997; Baltensperger 2003).

Table 3.2 The CT findings in acute osteomyelitis of the jaws

CT findings in acute osteomyelitis of the jaws (1–4 weeks after onset of disease)	
Acute osteomyelitis (within 2 weeks) • Rarification and loss of cancellous bone trabeculae • Demineralization, erosion, and thinning endosteal cortical plate • Loss of contour of mandibular canal and mental foramen • Osteolytic defect of cortical plate • Submandibular abscess/subperiosteal abscess	Acute osteomyelitis (3–4 weeks) • Sequester formation • Calcified periosteal reaction • Minor areas of cancellous bone sclerosis • Fracture as complication

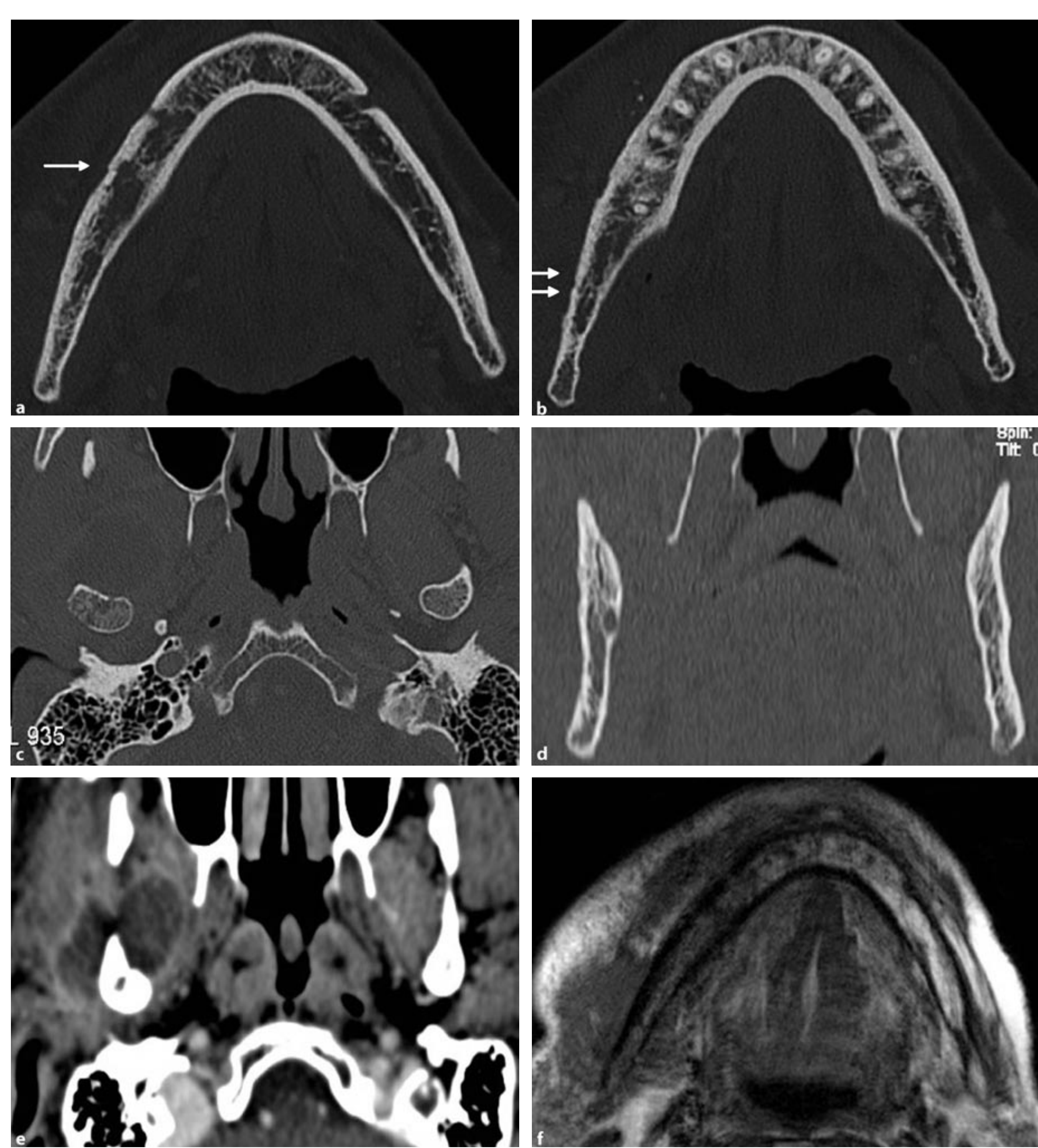
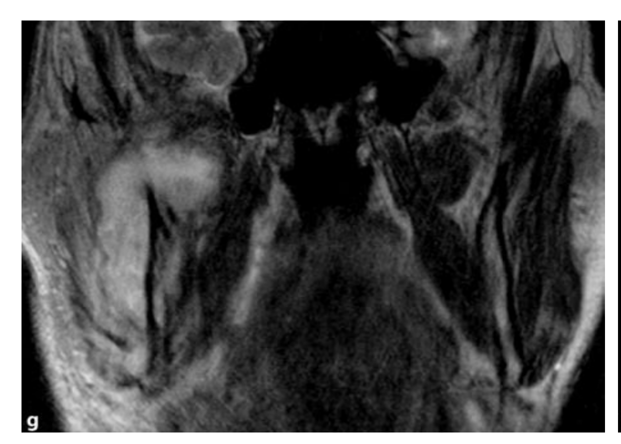


Fig. 3.5a–h Acute osteomyelitis with perimandibular infratemporal fossa abscess: a 54-year-old man with 2 weeks history of pain of right first molar and 4 days of progressive swelling of the right cheek with reduced mouth opening despite high-dose antibiotic treatment. Axial high-resolution bone-window CT images (**a–c**) depict cancellous bone osteolyis, loss of trabecular structure within right mandibular body and incipient buccal sequester formation region 47 (**a**, *arrow*). Small linear perforation through buccal cortical plate at mandibular angle is shown in **b** (*arrows*), demineralization and partial destruction of mandibular condyle is visualized in **c**. The limits of mesial extension (**b**) and the degree of involvement of the ascending ramus by intramedullary cancellous bone infection are hard to recognize (**d**). Axial CT with soft tissue window (**e**) displays perimandibular abscess at the level of the incisura semilunaris. Axial T1 MR image (**f**) from the same day reveals intramedullary low-signal tissue extending mesially to canine tooth revealing larger involvement of mandibular body than anticipated by CT. Slight buccal cortical plate narrowing and hyperintense signal indicates the site of sequester formation **g,h** *see next page*



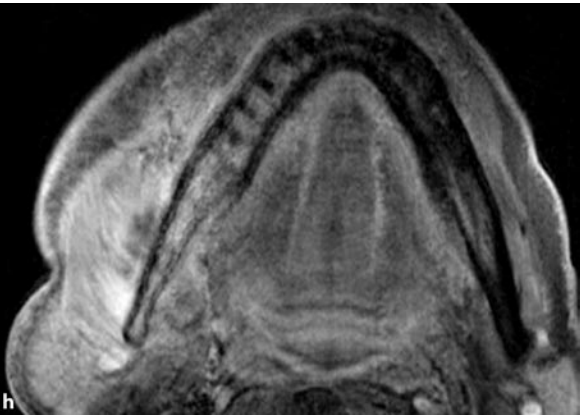


Fig. 3.5a–h (*continued*) Acute osteomyelitis with perimandibular infratemporal fossa abscess: a 54-year-old man with 2 weeks history of pain of right first molar and 4 days of progressive swelling of the right cheek with reduced mouth opening despite high-dose antibiotic treatment. Coronal T2 MR image (**g**) and axial Gd-enhanced, fat-suppressed T1 MR image (**h**) display increased cancellous bone signal within ramus and mandibular body. An abscess is shown that originates at the site of cortical perforation (**b**, *arrows*) to extend medial to masseter into semilunar incisure to reach the infratemporal fossa close to the skull base



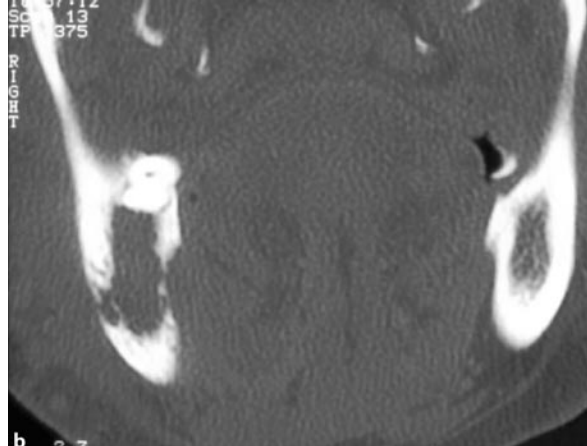


Fig. 3.6a–d Acute osteomyelitis and healing within 6 months after treatment: a 38-year-old man with 2 weeks history of pain, swelling and right chin hypesthesia following extraction of second right lower molar 3 weeks prior. Axial (**a**) and coronal (**b**) high-resolution bone-window CT images depict predominant cancellous bone destruction, endosteal lingual and buccal cortical bone demineralization and resorption. There is evidence of loss of contour of mandibular canal that serves as a pathway of extension of infection to the mental foramen, which is widened. **c,d** *see next page*



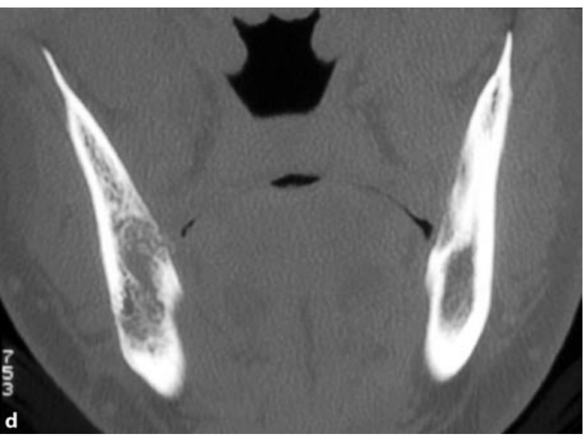


Fig. 3.6a–d (*continued*) Acute osteomyelitis and healing within 6 months after treatment: a 38-year-old man with 2 weeks history of pain, swelling and right chin hypesthesia following extraction of second right lower molar 3 weeks prior. Six months following decortication and initial antibiotic treatment, follow-up CT in the axial (**c**) and coronal (**d**) planes reveals osseous reconstitution of cancellous and cortical bone including the mandibular canal (Fig. 3.6a,c from Schuknecht et al. 1997)



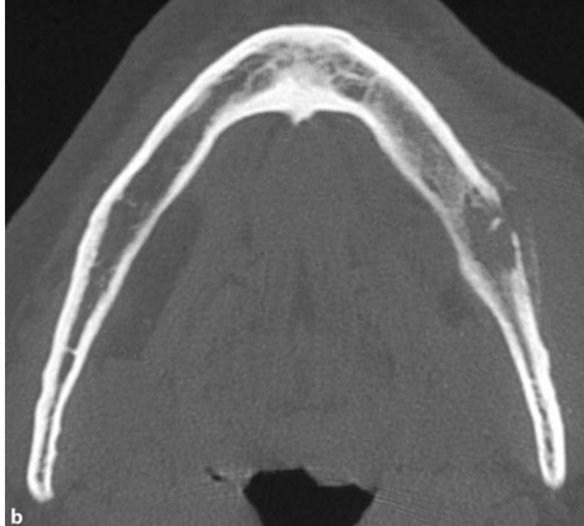


Fig. 3.7a,b Localized subacute-phase acute osteomyelitis with calcified periosteal reaction in a 47-year-old patient with 2 weeks history of mild pain but substantial swelling of left cheek 3 weeks following extraction of 36. Axial high-resolution bone-window CT images (**a,b**) depict osteomyelitis with cancellous bone osteolysis, buccal cortical plate perforation and linear calcified periosteal reaction. Periosteal calcification adjacent to a central cortical sequester is still incomplete. Note that cancellous bone sclerosis adjacent to empty alveolus 36 (**a**) indicates previous chronic inflammation. A barrier is thus provided that probably seals of intramedullary extension and consequently accounts for a more localized type of osteomyelitis (contrary to the case in Fig. 3.6) leading to early cortical bone penetration (Fig. 3.7a from Schuknecht et al. 1997)

In acute osteomyelitis the ramus is infrequently affected with numbers in the range of 7% (Calhoun et al. 1988) to 15% (Taher 1993). With 10% of manifestations the symphysis is a rare location as well (Ida et al. 1997), unless a fracture is the causative event (Adekeye and Cornah 1985).

A devitalized bone fragment which is dissolved from the adjacent cortical plate is called a "sequester." Sequester formation requires a minimum of 3 weeks of inflammation to be detected by CT (Fig. 3.5a). Computed tomography is more sensitive than conventional radiographs in recognizing the location and extent of sequester formation (Yoshiura et al. 1994). A "sequester" is usually found on the buccal side of the mandibular body and the adjacent ramus, and the symphysis is rarely affected. From the radiologist's point of view, contrary to current opinion, the occurrence of one or multiple sequester may not necessarily be a negative predictive factor indicating chronic transformation (Ida et al. 2005).

A periosteal bone reaction may cover the sequester and turn it into an "involucrum" (Fig. 3.8). The origin of new bone deposition is the cambium layer of the periosteum. Periosteal calcification may mask the recognition of a sequester or involucrum on conventional radiographs (Fig. 3.3a), and recognition therefore highly depends on CT.

Recognition of the location of a sequester aids in determining the extent of disease. In cases already positive on plain films, the precise extent of disease is a crucial question to be answered prior to surgery. The CT imaging thus supports the aim of surgery to remove all nonviable bone, but not to sacrifice more bone than necessary.

Inflammation and malignancy lead to different patterns of cortical bone CT changes in the majority of patients (Hariya et al. 2003). A permeative type of cortical bone destruction with numerous discontinuous defects was found in 10 of 12 patients (88.3%) harbouring metastatic disease to the mandible or lymphoma. In patients with osteomyelitis, this pattern occurred in one of nine instances only (11%). The presence of a periosteal reaction in 6 of 9 patients with osteomyelitis was an additional distinguishing factor. Periosteal new bone formation not only is disease dependent but is an age-dependent process as well. Particularly young patients exhibit a marked osteogenic potential of the inner cellular layer of the periosteum. The propensity to





Fig. 3.8a,b Advanced-stage acute osteomyelitis with involucrum formation and pathological fracture: a 23-year-old patient presents with sudden onset of pain and reduced mouth opening 2.5 weeks after drainage of a submandibular abscess, 4 weeks following extraction of 36 and 37. Axial (**a**) and coronal (**b**) high-resolution bone-window CT images depict an osteolytic area adjacent to empty tooth socket 37. Demineralization of lingual cortical bone is evident as well as buccal sequester formation covered by a linear periosteal bone reaction. This turns the sequester into a "involucrum." Sudden aggravation of symptoms is caused by a fracture. The lingual extension of the fracture line is shown between 35 and the well-demarcated socket 36, as well as along the lingual side of the mandibular ramus. (Figure 3.8a from Schuknecht et al. 1997)

develop a periosteal reaction is high in the young age group and lower in elderly patients irrespective of the potential malignant or inflammatory nature of the underlying disease.

A "periosteal reaction" occurs when the inner periosteal layer is affected by subperiosteal extent of disease. In osteomyelitis this may occur directly by inflammatory osteolysis (Fig. 3.7) or indirectly by extension of inflammation via Volkmann's vascular channels. The CT depicts a periosteal reaction as soon as calcified new bone is deposited. The process of periosteal calcification requires a minimum of 10–14 days. Periosteal reactions therefore relate to the advanced stage of acute osteomyelitis, predominantly in the third and fourth weeks after onset of the disease. A periosteal reaction was shown by CT in 40.2% (Ida et al. 1997) and 50% (Schuknecht et al. 1997) of patients. Ida et al. analysed the different patterns in 47 patients. In patients with osteomyelitis, a single or multi-layered appearance parallel to cortical bone was found in 91%, an irregular pattern was present in 3 cases (6.8%) and spiculae were noticed in a single patient (2.2%). Among patients with carcinoma metastases to the mandible, spiculae were the predominant manifestation in 11 of 18 patients (61.1%). With 16.7% a parallel and irregular pattern was the least common presentation (compare Figs. 3.7b and 3.14b with Fig. 3.17b,c). The incidence of periosteal reactions was identical in the group of patients with carcinoma metastases and the patients with osteomyelitis.

"Codman's triangle" is a triangular-shaped periosteal reaction that abuts an area of cortical osteolysis. Considered a sign of high malignancy, the frequency was 5.5% in patients with metastases to the jaw (Ida et al. 1997). Recognition of Codman's triangle or the spiculae type of periosteal reactions on CT requires considering a neoplasm or sarcoma rather than an underlying osteomyelitis. Periosteal reactions are considerably more frequently found in patients with sarcomas and carcinomas metastatic to bone rather than carcinomas infiltrating an adjacent segment of bone.

Periosteal reactions in patients with osteomyelitis may resemble a "Codman's triangle." When the periosteum is elevated by a circumscribed perforation of the cortical plate, a triangular calcification may develop along the lateral periosteal attachment displaying a "pseudo-" Codman's sign (Fig. 3.7a).

The periosteal reaction observed in patients with mandibular osteomyelitis may involve all nonalveolar borders, the body and angle lead in frequency (Figs. 3.3, 3.7). Periosteal reactions were predominant on the buccal aspect (80.9%), and the lingual or both sides were affected in 9.5% each (Ida et al. 1997). In another study a periosteal reaction was shown in 11 patients, affecting the buccal side in 5 (45%), the lingual side and both sides in three instances (27%) each (Schuknecht et al. 1997). Periosteal calcification may well extend from the angle along the ramus to the mandibular condyle (Fig. 3.3d,e). The lack or presence of periosteal calcification marks the transition from early acute (within the first 2 weeks) to the advanced phase (third and fourth weeks) within the acute stage of osteomyelitis (compare Figs. 3.3e and 3.5c).

Mandibular osteomyelitis may be accompanied by inflammatory thickening of the masseter muscle. On CT swelling and contrast enhancement of the muscle is found (Fig. 3.2b). Unless the rare situation of a submasseteric abscess is present (Fig. 3.5e–h), muscle swelling is more marked in the chronic rather than acute manifestations of osteomyelitis (compare with Figs. 3.9d and 3.14b). In patients with visible masseter enlargement, MRI is suited to distinguish abscess formation from infection-induced myo-tendinitis or the presence of an unrelated lesion such as an intramuscular venous angioma.

In 33 patients with mandibular osteomyelitis investigated by CT (Yoshiura et al. 1994), inflammation of the masseter muscle was present in 18 cases (54.5%), of the medial pterygoid muscle in 10 patients (30.3%) and the superficial temporal muscle in 5 cases (15.6%). In early and advanced stages of acute osteomyelitis soft tissue swelling along the body of the mandible or within the submandibular trigone is a frequent finding (Figs. 3.6, 3.7). The parapharyngeal space is rarely involved.

In summary, CT more closely reflects changes in osseous histology and the stage of disease than do conventional radiographs (Schuknecht and Valavanis 2003). This holds particularly true for assessment of cortical bone changes and recognition of calcified periosteal reactions which account for the majority of changes within the subacute phase of the acute osteomyelitis.

3.8 Magnetic Resonance Imaging

3.8.1 Examination Technique

The MRI examination protocol consists of a coronal and axial fast T2-weighted series that covers the upper and lower jaw, slice thickness is 3.5 mm. Axial and coronal T1-weighted series without and with gadolinium as contrast agent are additionally performed. The coronal T1-weighted series is replaced by a T1-weighted sagit-

tal oblique series in case of positive findings within the mandibular body or ramus on axial noncontrast images.

The contrast-enhanced series requires fat-suppression technique in order to facilitate recognition of pathological contrast enhancement within medullary bone and soft tissue.

Sagittal oblique T1-weighted contrast-enhanced images are performed in case of positive findings on the corresponding T1-weighted images only. Lee et al. (2003) advocate the use of short inversion time inversion recovery (STIR) images rather than fast T2-weighted images to depict diseased marrow. In an analysis of 29 patients with mandibular osteomyelitis, the sensitivity of STIR images is deemed better due to high signal in 75% of patients. In comparison, high signal was less frequently observed with 54% on fast T2-weighted images.

3.8.2 Findings

Magnetic resonance imaging plays an increasing role in the diagnosis of the early acute stage of osteomyelitis. Until recently the application of MRI in the maxillofacial region and mandible was not as well defined as in the appendicular skeleton.

An overview of the signs in MRI in acute osteomyelitis of the jaws is given in Table 3.3.

The high sensitivity of MRI in recognizing acute osteomyelitis is based on the ability to detect infiltration of fatty bone marrow. Medullary involvement pathologically is characterized by vascular engorgement, oedema, cellular infiltration and, finally, microabscess formation. Elevated water content accounts for increased signal on T2 and STIR images. The corresponding T1-weighted images demonstrate low signal intensity changes. In the context of cellulitis – the stage that precedes osteomyelitis – abnormalities of marrow signal may be subtle on both T2 and T1 images. More importantly, T1 images lack contrast enhancement.

In order to be called "osteomyelitis" contrast enhancement with signal increase is therefore required. The area of contrast enhancement corresponds to the low signal region on non-contrast images (Figs. 3.2d,e, 3.5f–h). In case significant oedema is present, the extent of T1 and T2 signal abnormality exceeds the location of contrast enhancement (Schuknecht et al. 1997; Schuknecht and Valavanis 2003).

Fat-suppression techniques allow better discrimination of the area of contrast enhancement from normal bone marrow. Persistent fat signal within the bone marrow on non-fat-suppressed MRI images has been described as a frequent finding in early acute osteomyelitis in the appendicular skeleton. Septic necrosis of bone marrow may result in the release of free fatty globules. Fat globules may aid in distinguishing early from advanced stages of acute osteomyelitis. While this refers to the appendicular skeleton (Davies et al. 2005), this finding has not yet been described for the mandible.

The interpretation of bone marrow abnormalities on MRI images has to take into account an age-related conversion of hematopoetic marrow into fat-containing cancellous bone. This commences within the mandibular body in the second decade of life. The angle and ramus follow in sequence until marrow conversion progressively reaches the mandibular condyle by the third decade (Yamada et al. 1995). Increasing replacement of hematopoietic by fatty tissue at least theoretically renders the diagnosis of acute osteomyelitis easier in adolescents and adults compared with young children. In this age group more specific signs lend favour to the diagnosis of osteomyelitis: these include focal bone destruction, periosteal reaction and sequestra formation.

The high sensitivity of MR in recognizing osteomyelitis has been confirmed by investigators using the standard field strength of 1.0–1.5 Tesla (T; Reinert et al.

Table 3.3 The MRI findings in acute osteomyelitis of the jaws

MRI findings in the acute osteomyelitis of the jaws (1–4 weeks after onset of disease)	
Acute osteomyelitis (within 2 weeks) • Replacement of marrow fat by inflammation • Enlargement of marrow space with thinning of cortical plate • T2 increase in signal intensity related to edema • T1 contrast enhancement due to blood tissue barrier disruption • Subperiosteal extension of inflammatory tissue • Noncalcified periosteal reaction • Subperiosteal/submandibular abscess	Acute osteomyelitis (within 3–4 weeks) • Dissolution of cortical bone fragments leading to sequester formation • Noncalcified periosteal reaction

1995; Köhnlein et al. 1997; Schuknecht et al 1997); however, even a low-field system of 0.2 T proved to be sufficient (Kaneda et al. 1995).

In the acute stage the sensitivity of MRI surpasses CT. In one study MRI findings were indicative of osteomyelitis in 4 of 4 patients (Kaneda et al. 1995). The CT examination had been false negative in 2 patients and conventional radiographs false negative in 4 of 4 patients in this study.

Magnetic resonance imaging outlines the intramedullary extent of inflammation earlier and more precisely than CT (Köhnlein et al.1997; Schuknecht et al. 1997). The explanation is the higher sensitivity of MRI in depicting a change in proton relaxation induced by the inflammation rather than the ability of CT to detect changes in radiodensity of trabecular bone (Fig. 3.2b–e). The activity and degree of inflammation as shown by histology appear to correlate with the intensity of contrast enhancement. Discrepancies were found in only 2 of 14 cases in which MRI overestimated the inflammatory "activity" compared with scintigraphy (Köhnlein et al. 1997).

The "penumbra" sign has been described as an additional finding related to the subacute phase of acute osteomyelitis (Davies et al. 2005). It consists of a peripheral zone of slightly elevated signal intensity on T1 images that surrounds the central bony abscess cavity. It corresponds to a layer of granulation tissue that lines the abscess cavity. The penumbra sign is bordered by a zone of peripheral oedema and of reactive new bone formation.

Increased intramedullary pressure contributes to the spread of infection into cortical bone via Haversian channels. Contrary to cancellous bone inflammation related to the early acute stage, MRI is less sensitive than CT in recognizing participation of compact bone. Cortical bone involvement predominates in the advanced stage of acute osteomyelitis. Sequestra exhibit low signal on T1- and T2-weighted images. This MRI appearance renders distinction difficult from the normal low-signal appearance of cortical bone (Fig. 3.5f–h). A direct sign of sequester formation is the interruption of compact bone by a high-signal rim on T2-weighted images and contrast enhancement on T1 sequences. The size of a sequester rarely exceeds the cortical bone of one tooth region. The location of a sequester may be a good indicator of the inciting tooth in case of large areas of intramedullary changes when the origin of an inflammation is difficult to pinpoint. Sequestra in general refer to the advanced phase of acute osteomyelitis and were detected earlier by CT as compared with MRI (Schuknecht et al. 1997).

Extension along Volkmann's channels or direct dissolution of compact bone allow inflammatory tissue to gain access to the subperiosteal space (Fig. 3.2c–e). Elevation and thickening of the periosteum result in marked contrast enhancement and thus recognition of a periosteal reaction – prior to calcification – at an earlier stage than by CT (Fig. 3.2e).

Via the subperiosteal space and the periosteum the inflammation may propagate to the adjacent soft tissues. Abscess formation may be within the vestibulum or more commonly descend into the submandibular trigone. Abscess formation may occur in a subperiostal perimandibular location below the muscles of mastication (see Fig. 3.5) or within the muscle fascia.

Magnetic resonance imaging showed soft tissue abnormalities in 10 of 14 patients (72%) with mandibular osteomyelitis compared with 3 patients (21%) by CT (Kaneda et al. 1995). Due to early detection of medullary bone and soft tissue involvement, MRI is deemed of high value to recognize and determine the extent of inflammation in acute and subacute osteomyelitis (Köhnlein et al. 1997; Schuknecht et al. 1997; Schuknecht and Valavanis 2003).

Magnetic resonance imaging may also be performed to differentiate an inflammatory from a neoplastic cause of an osteolytic lesion as depicted by conventional radiographs or CT. Multifocal separate lesions, lack of concomitant fat involvement and substantial focal soft tissue infiltration are signs favouring a neoplasm rather than an infectious process.

In summary, MRI is particularly sensitive in detecting acute osteomyelitis when the infection has reached the intramedullary cancellous bone, is able to delineate non-calcified periosteal reaction and to recognize the presence and extent of soft tissue infection.

3.9 Chronic Osteomyelitis: Conventional Radiology

Chronic osteomyelitis of the jaws may be the continuation of untreated or insufficiently treated acute osteomyelitis. In these instances it is referred to as secondary chronic osteomyelitis and is defined as a persisting infection of the bimaxillary skeleton that exceeds the time frame of 4 weeks.

Primary chronic osteomyelitis, on the other hand, is a chronic inflammation of the jaw of unclear aetiol-

ogy to date. The course of this rare disease is insidious, lacking an actual acute state. It is therefore considered "primarily" chronic. The clinical absence of pus, fistulae or sequestration is characteristic.

The two different manifestations of chronic osteomyelitis, primary and secondary chronic, are distinguished – both clinically and radiologically. Both types may present with episodes of quiescence and exacerbation.

The panoramic view is the standard examination – similar to the acute stage of osteomyelitis – to assess the osseous situation and the status of the dentition. Chronic osteomyelitis affecting the mandible is much better recognized than chronic osteomyelitis affecting the upper jaw. Suspicion for chronic osteomyelitis of the upper jaw therefore may require directly proceeding to a CT examination or, alternatively, apply additional radiographs like an occlusal view.

An overview of the signs in conventional radiology in secondary and primary osteomyelitis of the jaws is given in Table 3.4.

Chronic osteomyelitis of the jaws exhibits characteristic radiographic signs. The principle finding is progressive radiopacity with effacement of the trabecular structure of cancellous bone and loss of the cortical–cancellous bone interface. The radiographic signs histologically correspond to bone sclerosis with coarse trabeculae due to proliferation of osteoblasts rimming the bone trabeculae and encroaching on the marrow space. Areas of osteosclerosis may be accompanied by irregular relative radiolucencies. These correspond to small resorption defects that may be relatively cellular and well-vascularized. Conventional radiographs in a series of 27 patients (van Merkesteyn et al. 1988) with chronic mandibular osteomyelitis displayed a mixed sclerotic and lytic pattern in 17 cases (62.9%), and diffuse sclerosis was present in 10 patients (37%). In another study diffuse sclerosis was the main plain film presentation of chronic osteomyelitis in 50% of patients, and mixed sclerosis and osteolysis were found in 36% of patients (Kaneda et al. 1995). Radiolucent lines that interrupt an area of radiopaque cortical bone are indicative of sequestration (Fig. 3.8a,b), which may be masked otherwise due to the mixed presence of radiopacity and radiolucency (Fig. 3.4c,d).

Secondary chronic osteomyelitis may also be associated with sequester formation, whereas in cases of primary chronic osteomyelitis sequestration is always absent. In the aforementioned study (Kaneda et al. 1995) sequestra were encountered in 14% of patients.

Fistulae are related to secondary chronic osteomyelitis. Fistulae may indicate recurrence after previous decortication or may be observed in conjunction with sequester (Schuknecht et al. 1997). In primary chronic osteomyelitis fistula formation is missing.

Periosteal reactions are shown by plain films in 20% of patients (Schuknecht et al. 1997). When more extensive periosteal new bone formation is deposited a significant increase in the bucco-lingual diameter of the entire hemimandible may result (Ellis et al. 1977; Jacobsson et al. 1978; Hardt and Grau 1987; Felsberg et al. 1990). An increase in mandibular size is a characteristic feature of the "proliferative periostitis" (Ellis et al. 1977; Eisenbud et al. 1981). This manifestation of chronic osteomyelitis predominantly affects children and adolescents. Plain film findings consist of multilamellar periosteal appositions leading to marked thickening of cortical bone. Histology reveals sclerotic new bone deposition on the mandibular surface and wide trabecular spaces filled with a cellular connective tissue component. Periostitis ossificans is occasionally associated with the name of Garrè, a German surgeon who classified osteomyelitis into ten different manifestations at the end of the nineteenth century. Contrary to current opinion, however, Garrè's descriptions refer to acute osteomyelitis and none of his patients belonged

Table 3.4 Conventional radiological signs in secondary and primary chronic osteomyelitis of the jaws

Conventional radiological signs in secondary and primary chronic osteomyelitis of the jaws	
Secondary chronic osteomyelitis • Areas of increased radiopacity with loss of bone trabeculae • Minor areas of radiolucency, interruption of cortical bone • Sequester formation • Calcified periosteal reaction • Pathological fracture	Primary chronic osteomyelitis • Areas of increased radiopacity with loss of bone trabeculae, effacement of cortical–cancellous bone junction affecting a hemimandible • Minor spots of radiolucency • Rarely periosteal reaction • Temporo mandibular joint involvement

to the chronic stage (Garrè 1893; Wood et al. 1988; Baltensperger 2003; Schuknecht and Valavanis 2003). Osteomyelitis of the jaw was mentioned in three of his patients, two of whom were children.

Another manifestation of chronic osteomyelitis is termed "diffuse sclerosing osteomyelitis." It is encountered in older patients and on radiographs presents with increased radiopacity affecting edentulous portions of the jaws.

Diffuse bone radiopacity is the prominent finding in patients with the mandibular manifestation of "chronic recurrent multifocal osteomyelitis" (CRMO; Suei et al. 1995). The CRMO is a relapsing inflammatory disease and is considered a type of seronegative spondyloarthropathy. The prevalence of mandibular involvement is 2–8% (Schilling et al. 1999). It affects a variety of other bones such as the pelvis, sternum and scapula in addition to the originally described long bones. The disease is rare, accounting for 2–5% of all osteomyelitis cases, and primarily affects young girls, with a female/male ratio of 5:1 (Chun 2004). In a 5-year follow-up study of 23 patients, the median age of onset was 10 years with a reported range of 4–14 years.

An affiliation with another spondylarthropathy called SAPHO syndrome has been noted. First described by Chamot et al. (1986), this acronym is characterized by synovitis, acne, pustulosis, hyperostosis and osteitis. The radiographic appearance of the mandibular manifestation of SAPHO syndrome corresponds to "diffuse sclerosing osteomyelitis" (Farnam et al. 1984; Kahn et al. 1993; Suei et al. 1996). The prevalence of mandibular involvement in SAPHO syndrome has been reported to be similar to CRMO with 8.2% in a series of 85 patients (Kahn et al. 1994). While radiopacity governs the quiet phase of CRMO, areas of mottled cortical and cancellous bone osteolysis prevail during the episodes of recurrence. Small osteolytic lacunae that contain lymphocytes and plasma cells are potential sites of exacerbation leading to cortical erosion and periosteal reaction. Additional radiographs (and scintigraphy) aid in detecting synchronous or metachronous involvement of multiple bones such as the clavicle, humerus, radius, femur or tibia (Björksten et al. 1978; Probst et al. 1978; Stewart et al. 1994; Suei et al. 1994).

Primary chronic osteomyelitis displays a more uniform and extensive increase in radiopacity than the secondary chronic type (see Fig. 3.13). Increased cancellous bone density and cortical thickening causes the inner cortical contour and lamina dura of teeth to be effaced. Primary chronic osteomyelitis frequently commonly affects one hemimandible including the ramus and mandibular condyle. It has also been observed to be linked to SAPHO syndrome (see Fig. 3.14). Due to its occasionally expansile character (Ellis et al. 1977), the radiographic appearance may mimic fibrous dysplasia or osteoblastic metastases in adults (Worth and Stoneman 1977), cortical hyperostosis in infants and Ewing's sarcoma in childhood.

Terms like "diffuse sclerosing osteomyelitis," "chronic osteomyelitis with proliferative periostitis," and "chronic recurrent multifocal osteomyelitis" reflect the historically strong impact of both radiographs and histology on the nomenclature of the chronic types of osteomyelitis; however, the radiographic differences among these manifestations are probably arbitrary and represent a spectrum of the same disease when age-related factors, differing individual defence mechanisms or varying virulence of the infectious agent are taken into account.

The primary chronic type of osteomyelitis is characterized by a stable radiographic appearance which may undergo mild changes in case of relapse. Only in the secondary chronic type of osteomyelitis may a return of normal bone structure be expected when healing occurs (Bünger 1984; van Merkesteyn et al. 1988). As follow-up examinations, radiographs therefore also maintain a strong position.

In view of the non-specific clinical presentation of chronic osteomyelitis the primary intention to order conventional films is to delineate the extent of disease and provide evidence of its benign or malignant nature. The recommendation to perform biopsy when radiographs cast doubt on the diagnosis of osteomyelitis (Jacobsson 1984; Hudson 1993) should be modified unless CT or MRI provide further evidence of malignancy.

3.10 Scintigraphy and Positron Emission Tomography

Scintigraphy and positron emission tomography (PET) belong to the diagnostic procedures that use radionuclides to assess the presence and activity of chronic osteomyelitis. The accuracy of various diagnostic techniques to establish the diagnosis of chronic osteomyelitis of the appendicular skeleton was analysed in a meta-analysis of 23 studies (Termaat et al. 2005). Positron emission tomography was the most sensitive technique, with a sensitivity of 96% [95% confidence interval (CI): 88–99%] followed by scintigraphy with a sensitiv-

ity of 82% (95% CI: 70–89%) and 78% sensitivity for combined bone and leucocyte scintigraphy (95% CI: 72–83%). The sensitivity for MRI was comparably high with 84% (95% CI: 69–92%). Pooled specificity demonstrated highest values of 91% (95% CI: 81–95%) for PET, compared with 84% (95% CI: 75–90%) for combined bone and leucocyte scintigraphy, 60% (95% CI: 38–78%) for MR and the expectedly low specificity of 25% (95% CI: 16–36%) for bone scintigraphy; the latter is particularly affected by previous surgical or dental procedures. In chronic osteomyelitis scintigraphy may therefore be used to monitor the activity of the disease rather than to establish the diagnosis (Tsuchimochi et al. 1991; Groot et al. 1992; Rohlin 1993).

Scintigraphy is the diagnostic procedure of choice in detecting additional skeletal manifestations in chronic recurrent multifocal osteomyelitis and in patients suspected of having SAPHO syndrome (Zebedin et al. 1998). In both conditions, even in the absence of symptoms, bone scintigraphy detects additional sites of involvement (Suei et al. 1994).

Following conservative treatment recurrence of infection correlates with increased uptake, remission corresponds to decreased activity of the radio-pharmaceutical; however, even during phases of quiescence elevated activity may persist up to 4 months after symptoms have subsided (Tsuchimochi et al. 1991). The area of increased activity tended to be significantly larger than indicated by plain films (Rohlin 1993). Lesion size was also more extensive in three-phase ^{99m}Tc scintigraphy in 6 of 20 patients in comparison with MRI findings (Reinert et al. 1995). After successful treatment, simultaneous indium-111-labelled white blood cell/^{99m}Tc scintigraphy was found to return to normal much sooner than CT findings (Seabold et al 1995).

Scintigraphy and PET, and their role in imaging diagnosis of chronic osteomyelitis of the jaws, are given in Chaps. 4 and 5.

3.11 Computed Tomography

An overview of the signs in CT in secondary and primary chronic osteomyelitis of the jaws is given in Table 3.5.

Cancellous bone sclerosis and cortical bone thickening by endosteal and/or periosteal apposition are the cardinal CT changes that indicate the presence of the chronic stage of osteomyelitis. Calcified linear periosteal reaction and sequester formation may be additional findings. Clinically a suppurative course with fistula and abscess formation correlates with the CT presentation of secondary chronic osteomyelitis. CT findings consist of mixed sclerosis and osteolysis, sequester formation and/or cortical bone fistulae (Figs. 3.9a,b, 3.10). Sequester formation marks the transition from advanced stage acute to chronic osteomyelitis. Based on the observation that sequester formation is not only encountered in the chronic stage but in the late acute stage as well, it may be hypothesized that the transition from acute to chronic osteomyelitis probably occurs earlier than after the arbitrarily fixed limit of 4 weeks.

In secondary chronic osteomyelitis bone sclerosis may be accompanied by gross sequester formation and cortical erosion (Seabold et al. 1995). This was the case in 3 of 7 patients previously reported (Schuknecht et al. 1997). With the availability of CT the detection of sequestra improved from 45% on plain films to 91% (Orpe et al. 1996). As axial CT images precisely depict the bucco-lingual dimension of the mandibular body and ramus, attribution of a lesion like a sequester to the buccal or lingual side is easily accomplished (Fig. 3.9a,b). Sequester were found by CT between 4 weeks and 11 months following onset of symptoms. The buccal side was affected more often than the lingual side. Computed tomography therefore may direct surgical decortication more precisely to the correct side. After surgery and/or fracture, bone reconstitution leads to more dense-appearing new bone (Fig. 3.11). This appearance and the concomitant periosteal reaction

Table 3.5 The CT findings in secondary and primary chronic osteomyelitis of the jaws

CT findings in secondary and primary chronic osteomyelitis of the jaws	
Secondary chronic osteomyelitis • Areas of increased bone density, trabecular and cortical plate thickening • Areas of osteolysis, gross defects of cortical bone • Sequester formation, fistulae • Calcified periosteal reaction • Pathological fracture	Primary chronic osteomyelitis • Increased density of entire hemimandible • Loss of trabecular structure and effacement of cortical-cancellous bone junction • Minor osteolytic areas indicating infectious lacunae • (Rarely) periosteal reaction, mild bone enlargement • Temporo mandibular joint involvement

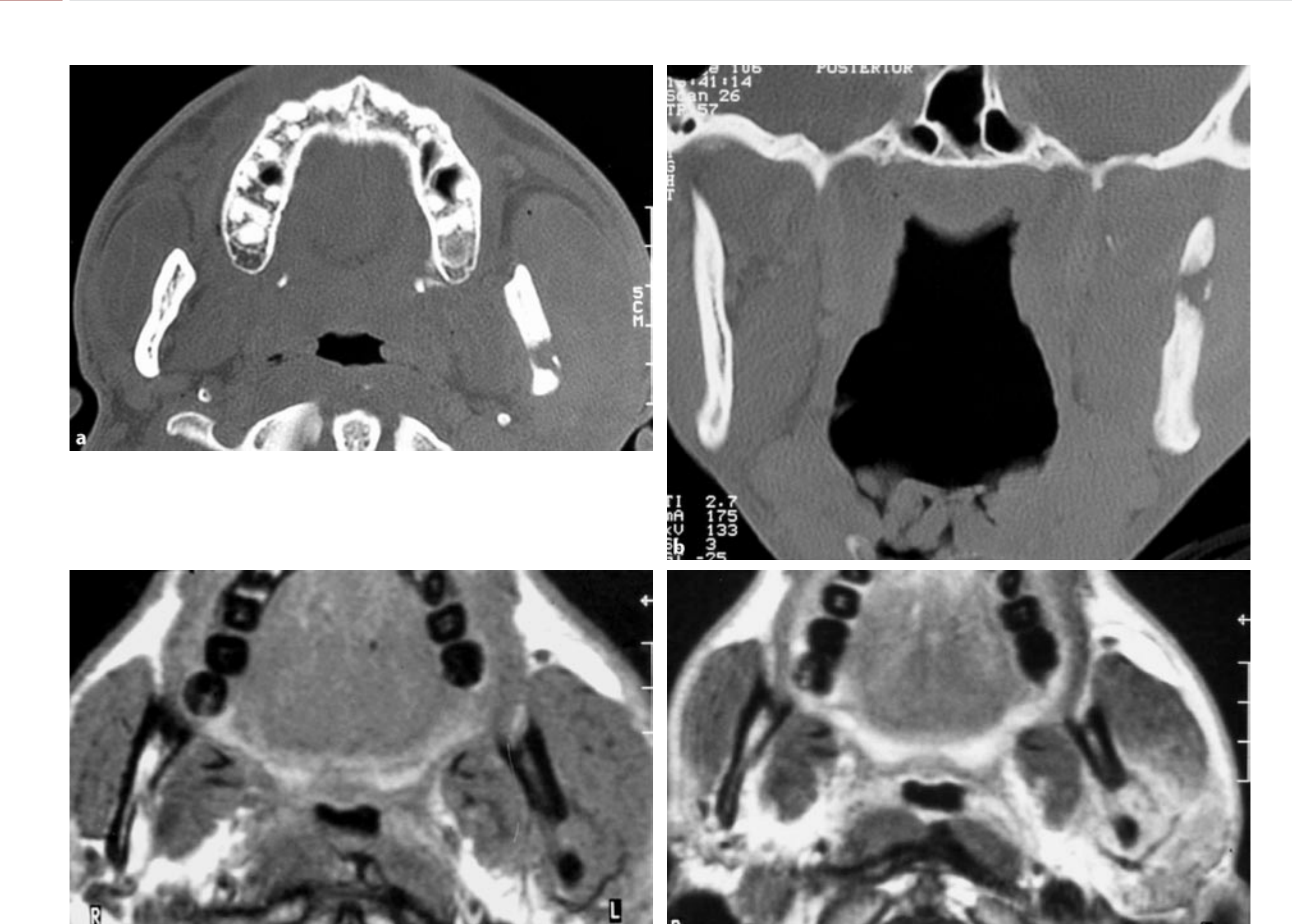


Fig. 3.9a–d Secondary chronic osteomyelitis: a 25-year-old man 11 months following tooth extraction and conservative treatment of perimandibular abscess. Axial (**a**) and coronal (**b**) high-resolution bone-window CT images depict left ascending ramus cancellous bone sclerosis and thickening, localized osteolysis with buccal sequester formation and marked thickening of masseter muscle. Non-contrast T1 MR image (**c**) and Gd-enhanced MR image (**d**) depict soft tissue infiltration along the posterior, medial and lateral aspect of the mandibular ramus centred on the osteolytic defect. Marked contrast enhancement of inflammatory tissue is shown extending on adjacent masseter muscle and along the lingual and buccal periost (Fig. 3.9c,d from Schuknecht et al. 1997)

have to be interpreted as normal on CT and watched over a period of 3 months unless strong clinical findings raise the suspicion of infection.

Periosteal reaction with ossification is a common finding in chronic osteomyelitis. It was shown by CT in 7 of 10 patients (Schuknecht et al. 1997), and in 11 of 11 patients (Orpe et al. 1996). When periosteal calcification is closely integrated into the cortical plate, it may not be recognized as periosteal calcification any more, but as mandibular cortical thickening (Figs. 3.9a,b, 3.14b). Periosteal new bone apposition thus causes mandibular enlargement. This is a particularly prominent feature when chronic osteomyelitis affects children or adolescents (Felsberg et al 1990; Ohlms et al. 1993; Stewart et al. 1994; Betts et al. 1996; Heggie 2000).

Medullary bone sclerosis is a constant marker in primary chronic osteomyelitis as well. Dense cancellous bone was present in 10 of 10 patients with chronic osteomyelitis (Schuknecht et al. 1997). In the so-called sclerotic pattern of osteomyelitis (Yoshiura et al. 1994) cancellous bone sclerosis depicted by CT presented as a diffuse process involving large areas of one hemimandible in 7 patients. The process was relatively localized in 3 cases only.

Increased density of medullary bone was found to extend as far as the coronoid process and mandibular



Fig. 3.10a–d Secondary chronic osteomyelitis with fistulation: a 74-year-old patient presenting with right suppurative fistulation into oral cavity and submandibular swelling following extensive decortication within right premolar area 7 months prior. On the axial (**a–c**) and coronal (**d**) high-resolution bone-window CT images an area of cancellous bone sclerosis is shown adjacent to the lingual decortication defect. Irregular osteolytic channels are seen medial to the mandibular canal (**c**). These fistulae tracts extend into basilar portion of mandible (**b**) and lead to lingual and vestibular perforation (**d**)

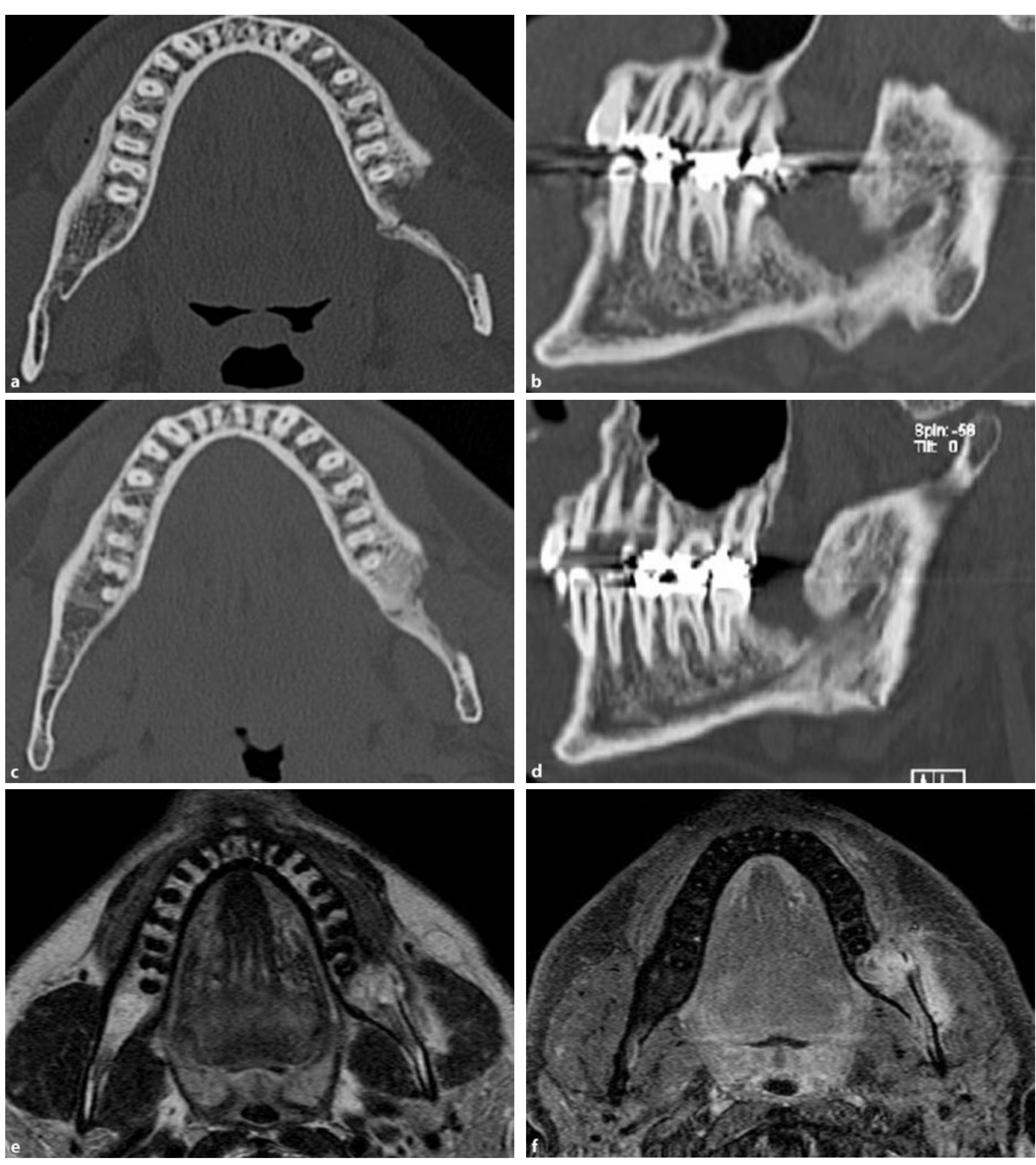


Fig. 3.11a–h Consolidating tissue response with new bone formation following surgical procedure and fracture (not osteomyelitis): a 45-year-old patient with mild pain and swelling 5 months following surgical removal of 38; follow-up examination after 3 months. Axial (**a,c**) and sagittal (**b,d**) high-resolution bone-window CT images depict extensive surgical defect following extraction of 38, a fracture traversing the basal mandibular cortical bone plate with adjacent periosteal reaction. The follow-up examination after 3 months (**c,d**) reveals osseous consolidation within resection site, smoothing of inferior mandibular periosteal contour and bridging of fracture. Non-contrast T2 MR images (**e,g**) and Gd-enhanced fat-suppressed MR images (**f,h**) were performed parallel to CT. The resection site is filled with inhomogeneous moderately bright tissue extending below masseter muscle (**e,f**). Posterior to resection site cancellous bone displays slight contrast enhancement leading to the interpretation of active granulation tissue versus delayed osteomyelitis. The follow-up examination displays complete resolution of soft tissue and reduction in size of resection area. **g,h** *see next page*



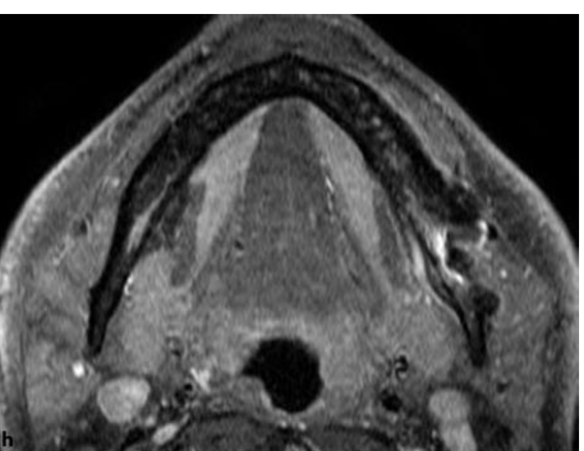


Fig. 3.11a–h (*continued*) Consolidating tissue response with new bone formation following surgical procedure and fracture (not osteomyelitis): a 45-year-old patient with mild pain and swelling 5 months following surgical removal of 38; follow-up examination after 3 months. *Bright line* in **h** corresponds to metallic artefacts originating from surgical instruments

condyle. The extent of mandibular sclerotic changes appears to correlate with the duration of disease. The sclerotic process does not remain limited to cancellous bone but causes endosteal cortical bone apposition leading to narrowing and osseous obliteration of the marrow space. Any compromise of the course and calibre of the mandibular canal is well recognized by CT (Figs. 3.12, 3.13c).

When a focal sclerotic lesion is restricted to the alveolar process florid osseous dysplasia is more likely than osteomyelitis (Groot et al. 1996). In primary chronic osteomyelitis of the mandible the inflammatory process appears to be of low activity and focussed on the endosteal and periosteal side of the cortical plate (Schuknecht et al. 1997). Absence of fistulae and sequestration are characteristic (Schuknecht et al. 1997; Baltensperger 2003; Baltensperger et al. 2004). A review of the CT findings in 78 patients with osteomyelitis – irrespective of the stage – attributed cancellous bone sclerosis, thickening of the cortical plate and increased mandibular diameter a negative impact on the chance of curability (Ida et al. 2005). Contrary to secondary chronic osteomyelitis, surgical treatment is not always the first choice and in some instances is deemed ineffective in the primary chronic type.

Increased size due to periosteal new bone apposition is an indicator of chronic or chronic recurrent inflammation (Suei et al. 1994; Schuknecht et al. 1997). Computed tomography attributes the clinical finding of mandibular swelling to an increase in bone volume (Betts et al. 1996; Heggie 2000). Increased mandibular dimensions are a characteristic though not specific finding in patients with SAPHO syndrome (Fig. 3.14). The mandibular ramus and condyle are frequently affected in conjunction with involvement of other bones and joints (Eyrich et al. 1999; Marsot-Dupuch 1999; Fleuridas et al. 2002). In addition to bone expansion, CT allows recognizing inflammation of the muscles of mastication, the masseter muscle in particular. The degree of swelling and contrast uptake may even be more pronounced than in the acute stage. Increasing volume and contrast enhancement of the masseter muscle is an early indicator of recurrence or exacerbation in chronic osteomyelitis (Orpe et al. 1996; Schuknecht et al. 1997).

3.11.1 Differential Diagnosis

Osteoradionecrosis may display similarity to chronic osteomyelitis on CT and radiographs (Fig. 3.15). Osteoradionecrosis of the mandible is a major concern in a patient who underwent radiation treatment for carcinoma of the oral cavity or oropharynx and after 1–3 years presents with exposed bone, a fracture or perimandibular swelling. Osteoradionecrosis, even though occasionally called radio-osteomyelitis (Calhoun et al. 1988; Koorbusch et al. 1992), is entirely different from true osteomyelitis in pathogenesis and presentation (Marx 1983). Osteoradionecrosis is induced primarily by hypovascularity due to vessel obliteration resulting in hypoxia and hypocellularity. Micro-organisms are

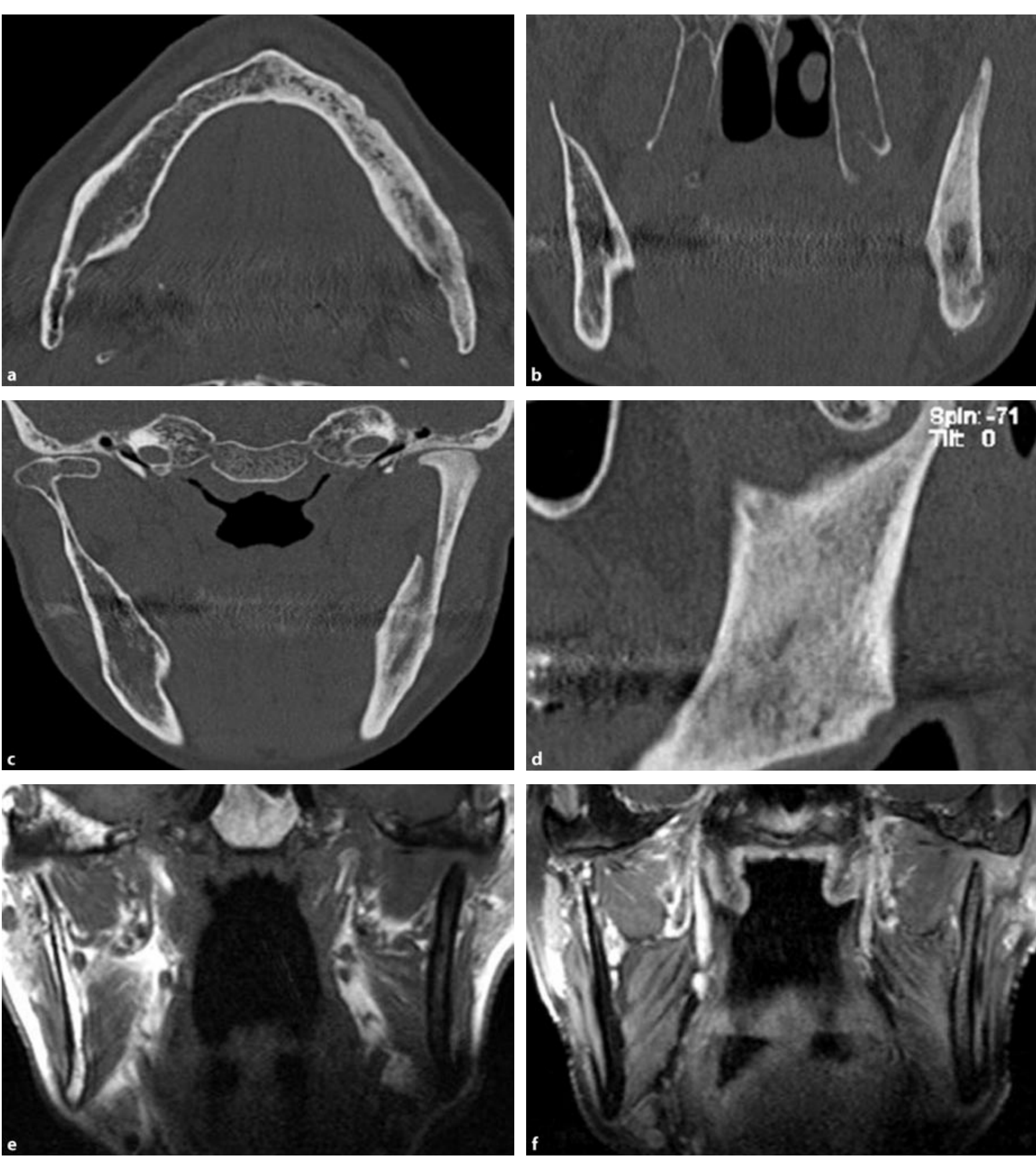


Fig. 3.12a–h Primary chronic osteomyelitis: a 47-year-old woman presents with reduced mouth opening. On retrospect, few episodes had been present with mild swelling of left cheek and slight pain. Axial (**a**), coronal (**b,c**) and sagittal (**d**) high-resolution bone-window CT images depict sclerosis of cancellous bone affecting the entire left hemimandible with an increase in size of ramus and coronoid process (**b**). Reduced dimension of sclerotic condyle is visible (**c**). Minor osteolytic zones are present at the angle (**b,d**) with cortical perforation (**b**) and slightly calcified periosteal reaction (**a,b**) indicating low-grade areas of inflammation. Coronal Non-contrast T1 MR images (**e,g**) display hypointense (*dark*) signal within cancellous bone of left ramus and condyle due to replacement of intramedullary fat by sclerotic tissue. Following contrast application, the Gd-enhanced, fat-suppressed MR images (**f,h**) reveal slightly elevated signal within marrow on the left indicating inflammatory activity, contrary to the fat-suppressed signal on the right side which stays dark. Additional inflammation is seen to affect the condyle and coronoid process **g,h** *see next page*

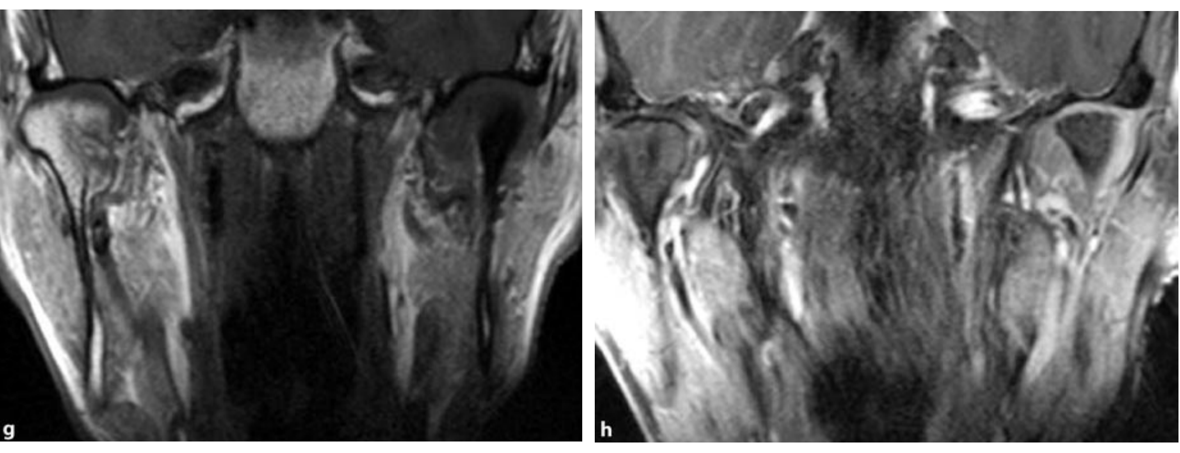


Fig. 3.12a–h (*continued*) Primary chronic osteomyelitis: a 47-year-old woman presents with reduced mouth opening. On retrospect, few episodes had been present with mild swelling of left cheek and slight pain.



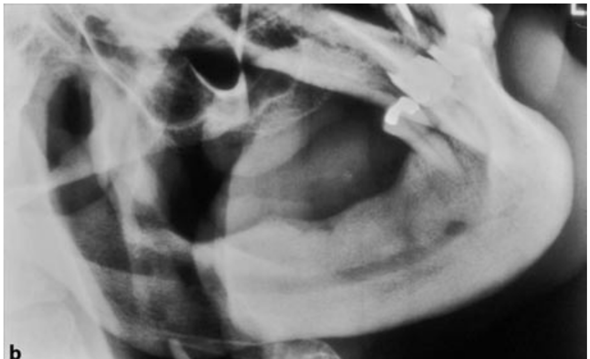


Fig. 3.13a–d Primary chronic osteomyelitis: a 61-year-old patient presents with mild pain and swelling of right mandible. Because of the same symptoms, extraction of right lower molar was performed 3 years prior. Buccal decortication within retromolar area had been undertaken 18 months prior. Mandible posteroanterior view and right oblique view (**a,b**) depict marked increase in radiopacity throughout the entire right hemimandible with the area of previous decortication well delineated.





Fig. 3.13a–d (*continued*) Primary chronic osteomyelitis: a 61-year-old patient presents with mild pain and swelling of right mandible. Because of the same symptoms, extraction of right lower molar was performed 3 years prior. Buccal decortication within retromolar area had been undertaken 18 months prior. Axial and coronal high-resolution bone-window CT images (**c,d**) reveal cancellous bone sclerosis with narrowing of mandibular canal as well as cortical thickening with a resultant increase in diameter of the mandibular body and ramus. Note sclerotic change of condyle with deconfiguration and arthrosis, probably a result of trophic changes





Fig. 3.14a,b Primary chronic osteomyelitis with incomplete SAPHO syndrome in conjunction with sterno-clavicular joint arthritis diagnosed by scintigraphy: a 10-year-old boy with progressive left mandibular swelling, recurrent episodes with fever and malaise and pain along the sternoclavicular joints. Mandible posteroanterior view (**a**) reveals a prominent well-delineated opacity resembling bone which projects along the buccal side of the mandibular angle. The entire ramus appears to be substantially increased in size. Axial high-resolution bone-window CT image (**b**) shows enlargement of ascending ramus with a linear periosteal reaction on the buccal and posterior side and small lacunae of decreased radiodensity within sclerotic cancellous bone. Note marked swelling of masseter muscle

Table 3.6 The MRI findings in secondary and primary chronic osteomyelitis of the jaws

MRI findings in secondary and primary chronic osteomyelitis of the jaws	
Secondary chronic osteomyelitis • Replacement of marrow fat by low-signal tissue with T2 increase in signal intensity related to oedema • T1 contrast enhancement due to major inflammation • Enlargement of marrow space with loss or thinning of cortical plate • Periosteal extension of inflammatory tissue, contrast-enhancing periosteal reaction • Soft tissue contrast enhancement	Primary chronic osteomyelitis • Replacement of marrow fat by T1 and T2 low-signal tissue • No signal change after contrast enhancement • Minor spots of bright T2 signal and contrast-enhancement as a sign of persistence or recurrence • Periosteal thickening with contrast enhancement indicating persistence or recurrence





Fig. 3.15a,b Histologically proven osteoradionecrosis without any signs of infection or tumours recurrence: a 63-year-old woman with a follow-up examination 1.5 years after surgery and radiotherapy of carcinoma of the tongue. Patient returns 15 months later because of sudden pain and mild swelling along left lower jaw. Axial high-resolution bone-window CT image (**a**) shows increased radiodensity within cancellous bone of mandibular body. A short segment of cortical bone had been resected on the lingual side. Follow-up CT after 15 months (**b**) displays a fracture line, lingual cortical defect and decreased density of cancellous bone distal to mental foramen

encountered as surface contaminants only, rather than infection-inducing agents.

Biphosphanate-induced osteonecrosis (osteochemonecrosis) has previously been reported in 119 patients treated for multiple myeloma, bone metastases of breast or prostate cancer and osteoporosis (Marx et al. 2005a). Clinically the patients presented with exposed bone of the mandible in 68.1%, the maxilla in 27.7% or both in 4.2%. The imaging findings in patients with biphosphanate-induced osteonecrosis have not yet been thoroughly investigated. A series of patients personally examined by CT and MRI presented with findings similar to primary chronic osteomyelitis. The CT findings consisted of marked sclerosis of cancellous and cortical bone without expansion but commonly with sequester-like fragments of bone. Cessation of bone remodelling and turnover by inhibition of the recruitment and activity of osteoclasts is the presumed mechanism (Marx et al. 2005a). The so-called bisphosphonate-related osteonecrosis probably represents a "pharmacologically"-induced osteopetrosis.

Marked sclerosis is the principle finding when the maxilla is affected; therefore, bisphosphonate drug treatment may be asked for before the diagnosis of a maxillary manifestation of primary chronic osteomyelitis is established. Another rare cause in the maxilla is invasive fungal infection (Fogarty et al. 2006).

The true osteopetrosis (Albers-Schönberg) is characterized by increased bone density and diameter due to osteoclast malfunction and on CT resembles primary

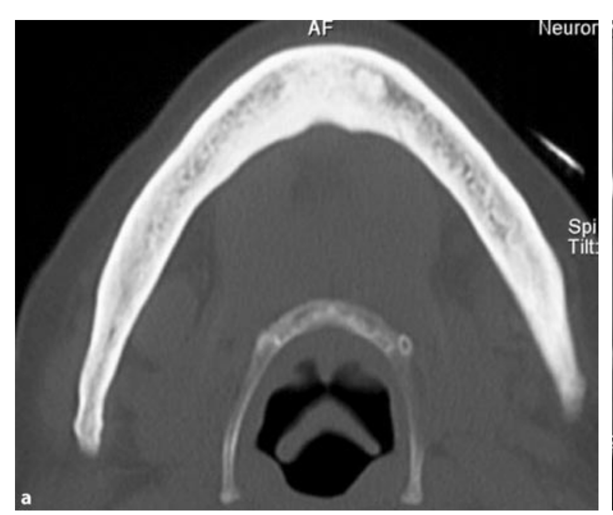




Fig. 3.16a,b Osteomyelosclerosis: a 51-year-old woman with a known systemic disease leading to pancytopaenia. Evaluation of the mid- and lower face because of trauma. Axial and coronal high-resolution bone-window CT images (**a,b**) reveal uniform increased density of cancellous bone without cortical plate involvement. Signs of primary chronic osteomyelitis (enlargement of bone, sparse minor osteolysis) or secondary chronic osteomyelitis (sequestra, fistulae and periosteal reactions) are missing

chronic osteomyelitis. Cancellous bone sclerosis is the dominant finding, and cortical bone is usually thickened (Barry 2003). While osteopetrosis is a known predisposing condition for osteomyelitis (Steiner et al. 1983), osteomyelosclerosis shows similarity to the appearance of primary chronic osteomyelitis both on radiographs and CT (Fig. 3.16).

Additional differential diagnostic considerations should include osteoblastic metastases related to carcinoma of the breast or prostate (Fig. 3.17).

In patients with chronic osteomyelitis, CT is recommended for staging and follow-up examinations. The CT allows discerning active from quiescent osteomyelitis, postoperative changes and reparative bony processes after successful therapy (Felsberg et al. 1990; Kaneda et al. 1995; Orpe et al. 1996). Computed tomography has also been advocated to recognize failure of surgical treatment (Sailer 1991; Montonen et al. 1993; Ida et al. 2005). Progressive diffuse sclerosis of the mandibular body most likely indicates insufficient decortication. Fracture of the remaining bone following decortication and pseudarthrosis formation signify increased vulnerability of sclerotic bone towards overuse, reduced healing potential, bone instability and/or infected reconstruction material. For correct interpretation of postoperative CT findings, knowledge of the type and extent of surgery and comparison with previous examinations are mandatory.

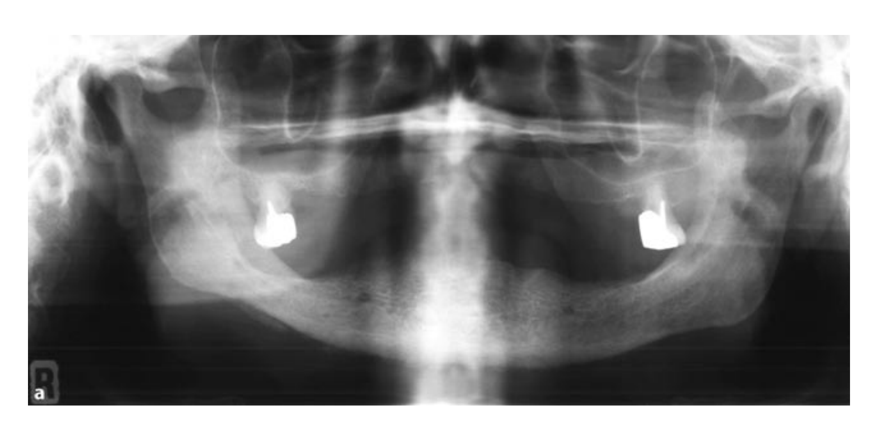
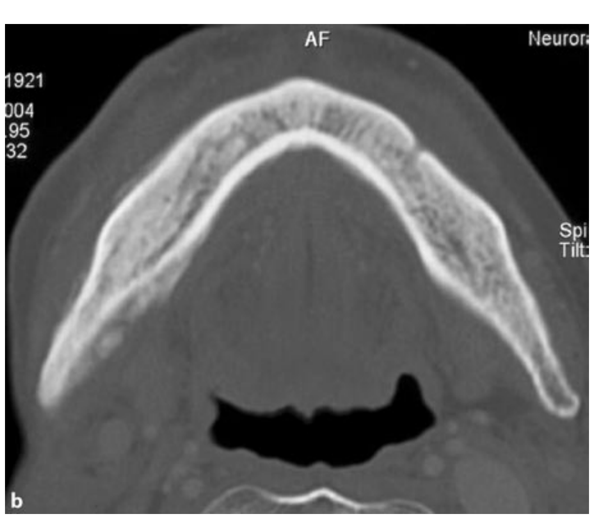


Fig. 3.17a–c Metastatic prostate cancer: an 83-year-old patient with pain and slight swelling along right mandible, hypesthesia of right chin. Panoramic view (**a**) shows alveolar atrophy and increased bone radiopacity more pronounced on the right. Furthermore, a prominent linear periosteal reaction is present extending along the basilar portion of right mandible. **b,c** *see next page*



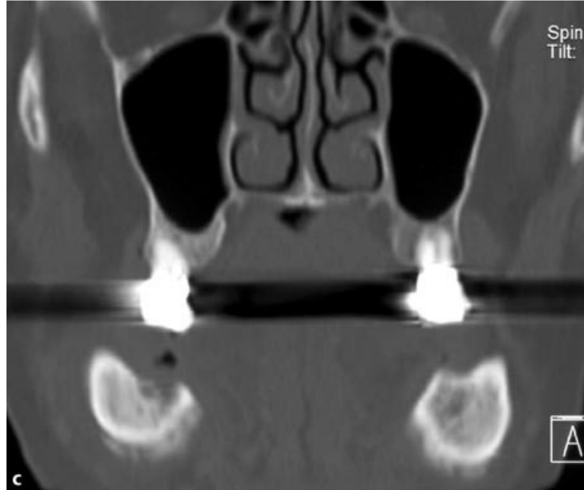


Fig. 3.17a–c (*continued*) Metastatic prostate cancer: an 83-year-old patient with pain and slight swelling along right mandible, hypesthesia of right chin. The axial and coronal high-resolution bone-window CT images (**b,c**) reveal marked sclerotic changes of medullary bone affecting the entire mandible. Furthermore, marked periosteal calcifications are presented bilaterally along with concomitant minor demineralization of the adjacent cortical plate

3.12 Magnetic Resonance Imaging

An overview of the signs in MRI in secondary and primary chronic osteomyelitis of the jaws is given in Table 3.6.

Magnetic resonance imaging offers the advantage of localising the infection within the medullary cavity in chronic osteomyelitis similar to the acute stage (Reinert et al. 1995; Köhnlein et al. 1997; Schuknecht et al. 1997). Magnetic resonance imaging thus exceeds CT in delineation of the intramedullary extent of disease. The location and extent are best displayed on T1 non-contrast images. The fat-containing bone marrow may be entirely replaced by pathological low (dark) signal. Contrary to acute osteomyelitis, the low signal also prevails on T2-weighted images. The reduced content of mobile protons in sclerotic cancellous bone accounts for these signal changes. The use of STIR images, rather than fast T2-weighted images, has been advocated in the depiction of diseased marrow (Lee et al. 2003).

Contrast enhancement is significantly less pronounced in chronic osteomyelitis compared with the acute stage (compare Fig. 3.12e and f with Figs. 3.2d and e). Fibrosis and sclerosis, which encroach upon the medullary space, result in decreased vascularity of cancellous bone. Alternatively, organisms of low virulence have been advocated to cause a continuous immune response (Eyrich et al. 1999) or an infection by *Actinomyces* species that triggers an immune response (Bartkowski et al. 1998). Due to the suggested low infectious activity with little inflammation in cases of primary chronic osteomyelitis, contrast enhancement as the sign of blood tissue barrier disruption is only minor. Contrast enhancement reveals lacunae of persistent infection as soon as they exceed 3 mm in size. The areas of recurrent infection within cancellous bone are therefore better delineated on MR, both in primary and secondary chronic osteomyelitis. Micro-abscess formation may be present, especially in cases of early-onset primary chronic osteomyelitis (Baltensperger et al. 2004), but infiltration of the marrow space occurs by lymphocytes and plasma cells (Wannfors and Hammerström 1985). T2 hyperintense (bright) signal and gadolinium enhancement therefore correspond to areas of persistent or recurrent active infection. In these cases contrast enhancement was found to correlate with histology in 10 patients (Kaneda et al. 1995). Discrepancies were attributed to sampling error, a temporal delay between imaging and histological assessment or misinterpretation of MR findings due to previous surgery or bone infarct.

The size of the lesions on MR frequently exceeds the size depicted by CT and scintigraphy. In comparison with scintigraphy, the extent of mandibular inflammation was larger on MR in 10 patients, equivalent in 4 and smaller in 6 patients (Reinert et al. 1995). The value

of MR thus may be deemed higher in guiding surgical debridement; however, restricted ability to visualize cortical bone limits the sole application of MR to define the area of decortication.

Cortical bone changes escape detection unless contrast media are applied. A short segment of cortical bone needs to be separated from the adjacent cortical plate by a line of contrast enhancement; however, lower spatial resolution due to thicker slices on MR compared with CT and the low cortical bone signal render detection of sequester more difficult on MR images (Schuknecht and Valavanis 2003). Commonly, sequester are only identified on MR images (Fig. 3.9c,d) in direct comparison with the corresponding CT slice (Fig. 3.9a,b).

Contrast application is also required to display inflammation of the periosteum (Reinert et al. 1995; Zebedin et al. 1998). Contrast enhancement of thickened periosteum is frequently accompanied by a mild degree of adjacent soft tissue enhancement (Figs. 3.2e, 3.9d). Thickened periosteum is a common finding in patients with primary chronic osteomyelitis (Schuknecht et al. 1997). The epi-periosteal space and the junction of the periosteum with the perimyseum of the masseter muscle appear to provide a pathway for the extension as well as the persistence of chronic inflammation (Flygare et al. 1997). Histology reveals lymphocytes and plasma cells to persist within the thickened periosteum and along the adjacent peri- and epimysium.

The degree of periosteal calcification, however, is difficult to assess unless the periosteum is entirely ossified. Calcification of the periosteum is therefore recognized in an advanced stage only. It presents as a hypointense line on T2-weighted images (Flygare et al. 1997) merged with the contour of the cortical plate. Preoperative delineation of chronic periosteal inflammation by MRI means recognition of a nutritional barrier that requires resection as long as it is not entirely ossified (Sailer 1991). Magnetic resonance imaging is of particular value to define the location and degree of persistent periosteal inflammation.

The purpose of surgical intervention is to remove sequester, infected bone and periosteal granulation tissue by decortication to stimulate revascularization. While sequester and bone islands are readily delineated by CT, periosteal inflammation and lacunae likely to maintain infection are depicted to better advantage by MRI.

Following surgery, the resultant soft tissue changes and persistent contrast enhancement along the site of decortication or bone resection render adequate assessment difficult (Fig. 3.11). Furthermore, artefacts may be present when osteosynthetic material has been used or as a result of drilling (Fig. 3.11h). Minor metallic residues inadvertently are left behind and alter the local magnetic field. This may cause MR images to be degraded. Immediately following surgery, MRI is of questionable value for 3–6 months until marrow and periosteal changes have subsided. After a delay of 6 months, MR is better suited than CT in detecting ongoing or recurrent infection.

Long-term follow-up of patients with chronic osteomyelitis requires cross-sectional imaging. Designating the patient as "cured" or "non-cured" based on imaging as an additional criterion may lead to a different result when compared with an approach based more on the clinical status and conventional radiographs. With CT images as additional factor (Ida et al. 2005) 29 of 78 patients with chronic osteomyelitis (37%) were judged as non-cured. This is a higher number than the proportion of 5 of 30 patients (16.7%) defined as "non-cured" by Baltensperger et al. (2004).

A change in the clinical status of a patient with chronic osteomyelitis may indicate recurrence or a complication such as a fracture or rarely conversion of chronic inflammation into a squamous cell carcinoma. Judged as a late complication of chronic osteomyelitis the incidence is estimated to be 0.2–1.5% (Hudson 1993). Magnetic resonance imaging is preferred over CT to define the location and extent of a carcinoma which is much more likely arising "de novo" related to the same risk factors than by transformation of chronic infection.

3.13 Bisphosphonate-related Osteonecrosis of the Jaw and Secondary Chronic Osteomyelitis

Bisphosphonate-related osteonecrosis of the jaws (BRON) has increasingly been recognized since 2003 as an adverse effect of bisphosphonate treatment (Marx 2003). Bisphosphonates have evolved as standard regimen for treatment of osteolytic bone lesions related to multiple myeloma and osseous metastases of solid cancer, carcinoma of the breast and prostate in particular. Treatment with bisphosphonates has proved beneficial in decreasing bone pain, reducing the risk of pathological fracture and eliminating malignancy-induced hypercalcaemia. The majority of oral prescriptions are for prevention of complications related to osteoporosis (Marx et al. 2005b).

The occurrence of BRON depends on the type and administration (oral vs. intravenous) of bisphospho-

nates, and the duration of treatment. Bisphosphonates act by inhibition of osteoclast-mediated bone turnover and renewal. As synthetic analogues of inorganic pyrophosphate, bisphosphonates are incorporated into the hydroxyl-apatite matrix at sites of active bone remodelling and into periodontal structures. The osteoclast inhibitory and anti-resorptive effect leads to prolonged secondary mineralization, increase in mineral density and mild augmentation of bone matrix.

As mentioned previously, BRON is considered to be a condition which facilitates secondary bone infection. The differential diagnosis of (secondary) chronic osteomyelitis requires including BRON due to similarities in clinical and imaging presentation. The classical clinical presentation of BRON consists of areas of exposed bone and non-healing extraction sockets often complicated by secondary infection (Dannemann et al. 2007). Tooth extraction, surgery, biopsy and pressure exerted by prosthesis have been implicated as inciting factors (Ruggiero et al. 2004). Superimposed chronic bone infection may lead to periosteal involvement, formation of sequestra and development of oro-antral and extraoral fistulae; these are expected to alter the clinical presentation as well as imaging manifestation.

The diagnosis of BRON is based on the history of bisphosphonate treatment, a thorough intraoral clinical examination and imaging evaluation of the jaws. Imaging characteristics may be subdivided into those related to the bisphosphonate substance and findings caused by secondary infection (e.g. superimposed secondary chronic osteomyelitis) at sites of exposed bone, extraction sockets and surgical intervention.

Signs of bisphosphonate incorporation include areas of sclerosis, thickening of the lamina dura and mandibular canal and cortical bone prominence leading to mandibular enlargement.

Prior to clinical manifestation, the initial signs may be negative or subtle (Fig. 3.18a) Bisphosphonate incorporation is visualized by thickening and prominence of the lamina dura, and of the cortical confines of the mandibular canal. These signs have to be scrutinized on the OPG. The OPG is obligatory to assess the dental status,

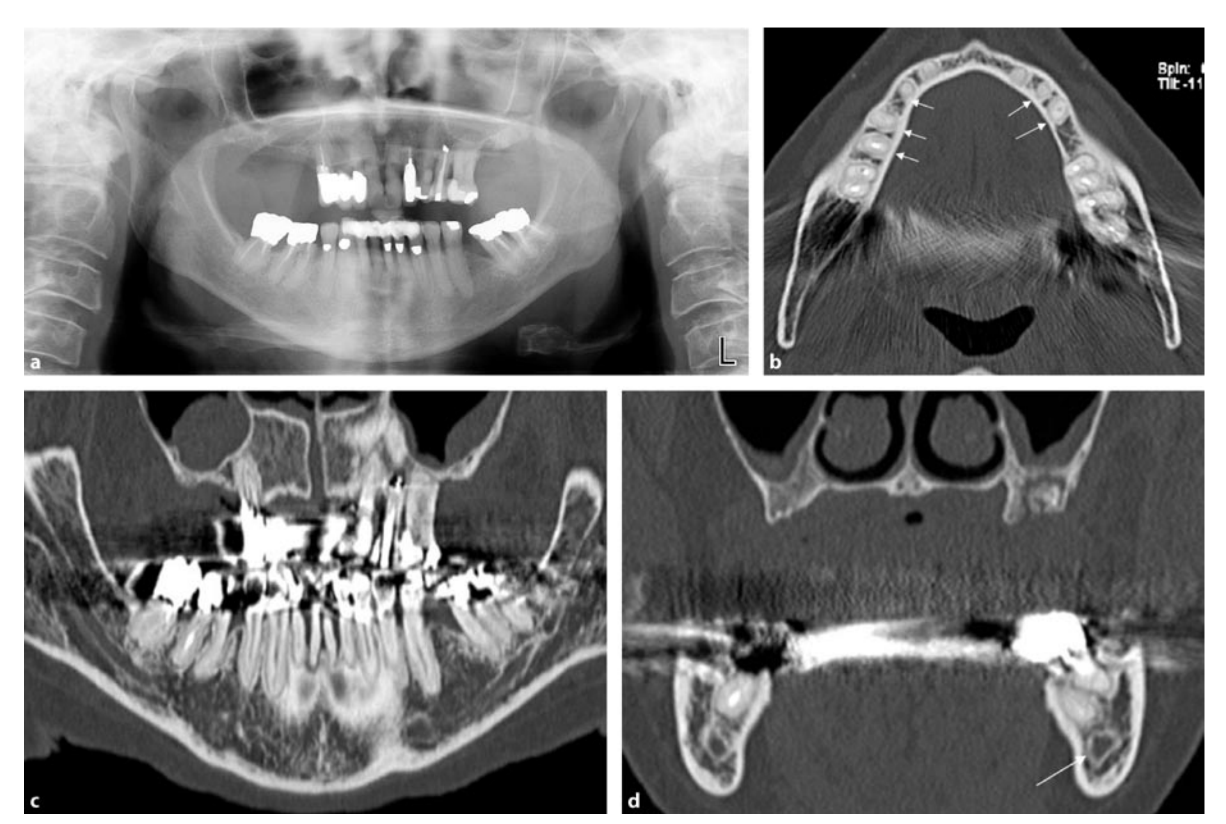


Fig. 3.18a–d Patient with bisphosphonate-induced osteochemonecrosis of the jaws. Secondary chronic osteomyelitis of the left maxilla with sequester formation (**d**). Note prominent sclerosis around the mandibular canal (**c**, *arrow* in **d**) and improved delineation of a prominent lamina dura (**c**, *arrows* in **b**) as signs of BRON in the mandible

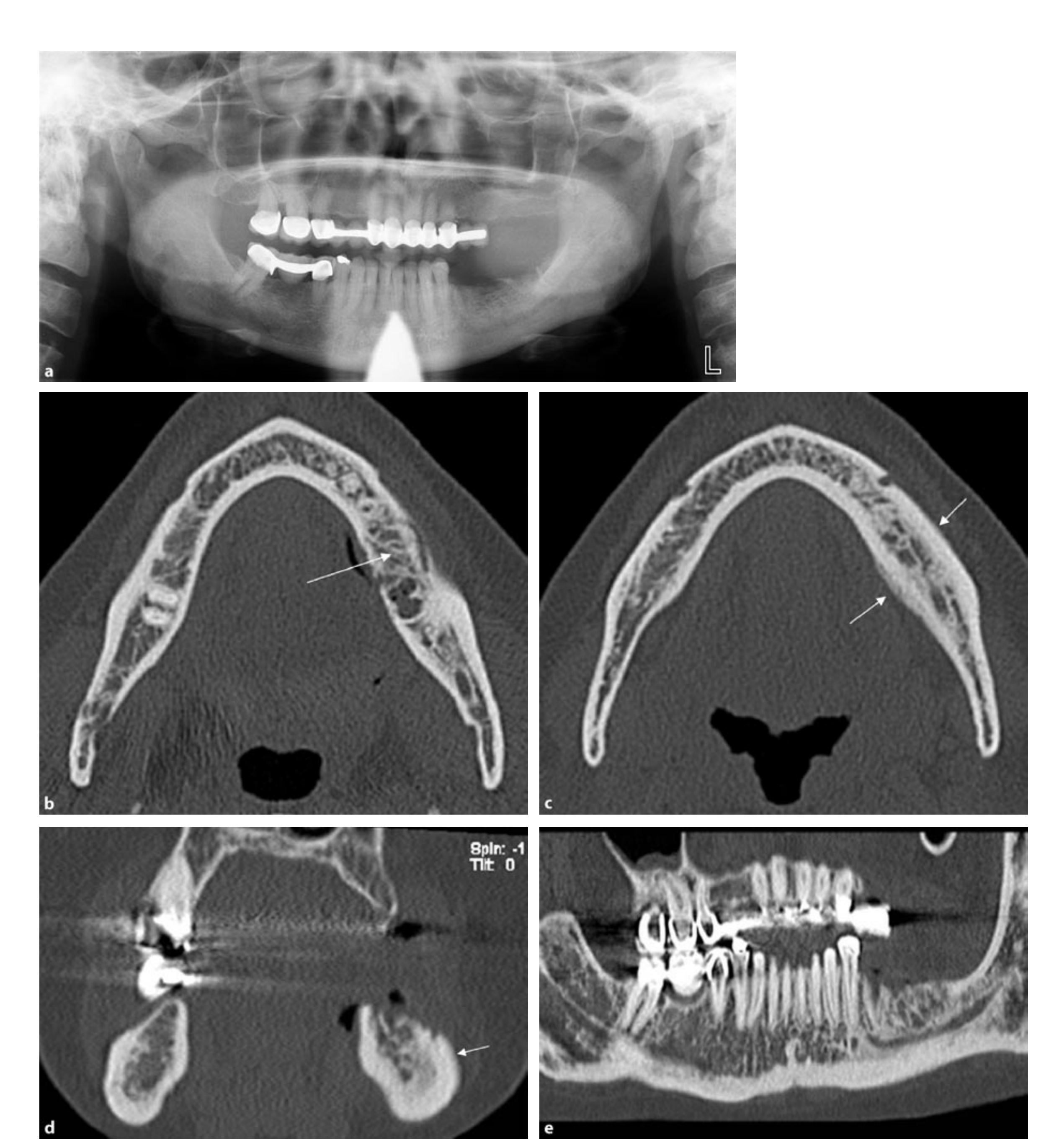


Fig. 3.19a–e Patient with bisphosphonate-induced osteochemonecrosis of the jaws and secondary chronic osteomyelitis of the left mandible. While the OPG (**a**) only shows a beginning osteolysis of the alveolar bone of the left mandible, corresponding CT scans demonstrate a beginning sequester formation (*arrow*, **b**) and periosteal reaction (*arrows*, **c**,**d**). Note prominent sclerosis around the mandibular canal and improved delineation of a prominent lamina dura as signs of BRON in the mandible (**e**)

exclude a fracture at sites of extraction sockets and may also be normal. In case of uncertainty a comparison with a previous OPG examination – if available – is helpful; otherwise, a CT examination with particular reference to these features is more sensitive provided that a high-resolution bone window algorithm examination has been performed and a radiologist with particular experience in dento-maxillo-facial imaging is involved. The initial contention was that osteolytic lesions supervene on the OPG in particular (Chiandussi et al. 2006). In a series of 119 patients positive radiographic findings were encountered in 73.1% (87 of 119): 85 patients displayed osteolysis combined with osteosclerosis. Osteosclerosis alone was found in 2 cases (Marx et al. 2005b). More commonly radiolucency corresponds to marked infection in conjunction with an area of osteonecrosis. Purely osteolytic lesions more likely are due to metastasis or recurrence in case of multiple myeloma.

According to own data in 38 patients the mandible is affected in 76% of cases, the maxilla in 18% and both jaws in 6%. Computed tomography may add information with respect to improved delineation of a prominent lamina dura, thickening of the mandibular canal and enlargement of cortical bone. A "curved" reconstruction corresponding to an OPG-like image is particularly helpful in assessing the early signs (Fig. 3.18b–d).

Osteosclerosis is the hallmark of BRON that first affects the alveolar bone in areas of previous tooth extraction, surgery or implant placement. Sclerosis extends into cancellous bone and is a definitive sign of BRON on the OPG or CT (Fig. 3.19), when an alveolar–basal gradient of sclerosis is evident. Preferential involvement of the alveolar portion of the mandible indicates inhibited remodelling where the requirements of bone renewal are more pronounced than in the basal mandible. It is visible on the OPG, coronal CT images or on OPG-like CT reconstructions. This "gradient" is missed in the maxilla.

Marked areas of sclerosis are only initially bound to sites of previous dental treatment and secondarily may extend to affect the tooth-baring portion of an entire hemimandible or the entire jaw. Resemblance to primary chronic osteomyelitis is given in this stage.

Signs of infection are concomitantly frequently present. On imaging infection is indicated by sequestra, fistulae and periosteal calcification. A sequester (Fig. 3.19a) may not be visible on the OPG due to periosteal calcification hiding the sequester as an involucrum. The OPG is frequently insensitive to recognition of sequestra in the maxilla in particular. Computed tomography is required to confirm sequestra, oro-antral communications and depict the extent of osseous involvement (Fig. 3.20). Periosteal calcification, even when subtle, is frequently visualized on CT images (Fig. 3.19b–e). Persistent inflammation may result in marked thickening of cortical bone and thus may imitate secondary chronic osteomyelitis. Small fistulae escape detection on the OPG but may be well delineated on CT. While the role of CT is already established (Phal et al. 2007), MR imaging is preferentially performed as a supplementary technique. Based on our experience with CT and MR imaging in 25 consecutive patients, MR depicts the degree of involvement of cancellous bone by infection. Magnetic resonance is thus of similar importance as in recognizing the acute stage of osteomyelitis and in delineating recurrence in primary chronic osteomyelitis.

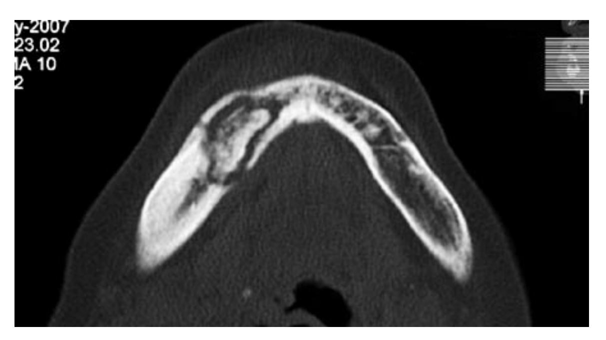


Fig. 3.20 Osteochemonecrosis with secondary chronic osteomyelitis and sequester and fistula formation in a patient with bisphosphonate therapy (Courtesy of C. Jaquiéry)

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Diagnostic Imaging – Scintigraphy

4

Nicolas Hardt, Bernhard Hofer, Marc Baltensperger

Contents

4.1 Summary

Scintigraphy is a well-recognized tool in the early diagnosis osteomyelitis of the jaws. Due to the sensitivity of this investigation, the extent of the infectious lesion can be determined accurately and hence give important information prior to surgical therapy. An additional useful feature of bone scans is their ability to monitor activity during the course of the disease and hence determine the effectiveness of therapy as well as detecting relapse.

Although high-resolution CT and especially MRI scans have reached a level of sensitivity which allow them well to compete with scintigraphic investigations, in certain instances they cannot fully replace this technology. In cases of syndrome-associated primary chronic osteomyelitis scintigraphy is recommended to detect possible multifocal skeletal lesions such as in chronic recurrent multifocal osteomyelitis and SAPHO syndrome.

4.2 Basic Considerations of Pathological Anatomy

In an early stage of disease, inflammations of jawbones are confined primarily to soft tissue within the bones (marrow), more than to the avascular calcified osseous matrix. The rich vascularization and low resistance of this tissue facilitates initial spreading of the pathological process within the bone (Brosch 1964; Doerr and Uehlinger 1966; Härle 1980). The osseous matrix is involved secondarily in the inflammatory cascade. With progression of inflammation, granulation tissue is formed, which jeopardizes local perfusion and eventually leads to necrosis of the bone, initiating a cascade of osteoclastic and osteoblastic bone activities.

Osteolysis is the result of increased osteoclastic activity. The osteoclasts, as the cells primarily responsible for this action, arise from the developed granulation tissue. Shortly after the initiation of bone destruction, reactive new endosteal and periosteal bone formation appears as an attempt of the host to isolate the region of infection; hence, in every inflammation involving bone there is always a very active turnover of tissue with a continuous change of microstructure (Adler 1997).

4.3 Different Types of Osteomyelitis

The clinical course of acute and secondary chronic osteomyelitis depends on the interaction of virulence of the infectious agent with local and systemic host factors

(Hardt and Hofer 1988; Hardt 2000, 2003; Eyrich et al. 2002; Baltensperger et al. 2004).

According to pathological–anatomical changes of the bone tissue and the clinical course of the disease, three major types of osteomyelitis are distinguished: acute and secondary chronic osteomyelitis as well as primary chronic osteomyelitis (Fig. 4.1). The first two types, as described in extent in Chap. 2, represent the same disease at different stages after onset of infection. Namely, secondary chronic osteomyelitis is a prolonged course of acute osteomyelitis due to late diagnoses and/or refractoriness to (inadequate) treatment. Primary chronic osteomyelitis, on the other hand, is considered a separate disease entity. Acute and secondary chronic osteomyelitis are suppurative infections, whereas primary chronic osteomyelitis is, by definition, a nonsuppurative bone disease. The pathological anatomy of acute and secondary chronic osteomyelitis may differ widely covering the full range of bone reaction; hence, predominant osteolysis and bone necrosis with sequester formation are observed in advanced acute stages as in chronic cases of high intensity, whereas diffuse sclerosis and increased bone volume due to periosteal and endosteal bone apposition are more often seen in chronic forms with a less intense course. These changes in presentation may occur at any time during the course of the disease depending on virulence of the causative bacteria and host factors (Obwegeser and Sailer 1978).

In acute osteomyelitis the central lesion consists of necrotic bone surrounded by a zone of predominant osteolysis. With the prolonged course of the disease a peripheral zone, dominated by osteoblastic activity, is created (Mercuri 1991). With adequate therapy and a sufficient immunological host response a cure can be achieved in an early stage of the disease. If not treated sufficiently, secondary chronic osteomyelitis will prevail with ongoing resorption and repair of the infected bone (Fig. 4.2; Hardt and Hofer 1988).

Primary chronic osteomyelitis is an inflammatory disease of the jaw of unknown origin. Low-grade infection and other autoimmunological mechanisms are considered causative. In primary chronic osteomyelitis the predominant tissue reaction is sclerosis. In some cases this may lead to a significant periosteal reaction mimicking a bone tumor. Furthermore, multiple regions of bone osteolysis may be noted infrequently. They are usually interpreted as a sign of increased disease activity (Fig. 4.2; Eyrich et al. 2003; Baltensperger et al. 2004).

4.4 Scintigraphy: Basic Considerations

In skeletal scintigraphy the basic principle consists of injecting a radioactive tracer into the circulation system. Radiopharmaceuticals that are absorbed by bone provide particularly useful information. In most applications ^{99m}Tc-labeled methylene diphosphonate is administered intravenously. The complete ^{99m}Tc bone scan consists of three phases. The first phase (flow study) consists of serial 3- to 4-s images taken during the first 1–2 min after injection of the radionuclide. The second phase (blood-pool study) consists of a single image obtained 5–10 min after injection. The third phase (delayed study or bone study) includes multiple views obtained 2–4 h after injection (Gold 1991). The tracer is embedded into the newly formed bone tissue; hence, uptake is directly proportional to osteoblastic activity. This type of bone scanning is therefore suitable for detecting not only the absolute activity of bone metabolism but perhaps even more importantly it allows demonstration of

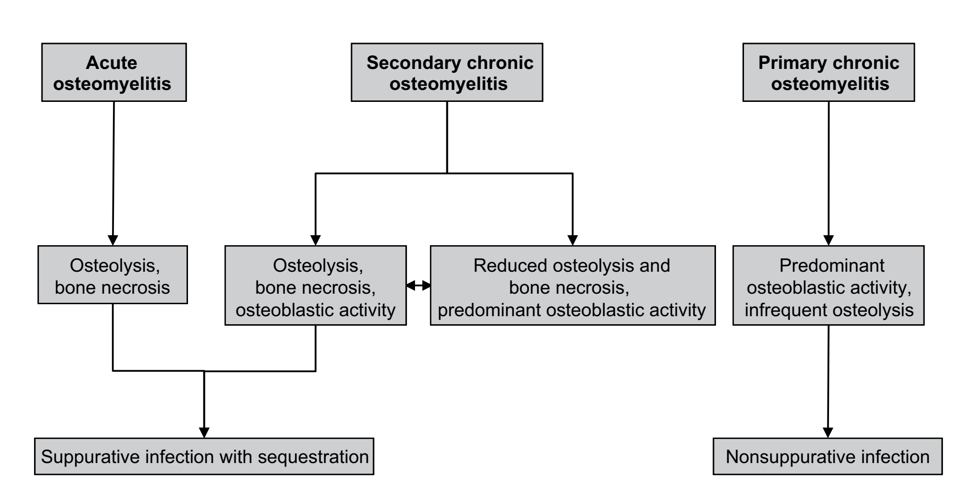


Fig. 4.1 Major groups of osteomyelitis and their clinical and radiological manifestations

relative regional differences of activity (Hardt and Hofer 1988; Bessler 1985).

Because administration of an additional radiopharmaceutical always increases exposition of the patient to radioactivity, these scintigraphic investigations should only be used when a clear diagnostic benefit is expected. Examination of several scan phases does not increase radioactive exposure of the patient, because no additional tracer needs to be injected; however, the examination time is increased, making it more impractical as an outpatient procedure. By examination of several consecutive phases of the scan acute osteomyelitis can be differentiated from chronic forms by a positive early phase in the former compared with negative early phases in the latter. Further information regarding distribution of a lesion is obtained using this technique. In an early phase (blood-pool study) soft tissue surrounding the infected bone can be assessed. This can give additional valuable information concerning involvement of these tissues in the infectious process.

Standard bone scintigraphic images of healthy individuals usually demonstrate a symmetrical distribution pattern among corresponding bones. A homogenous distribution throughout the entire skeleton, however, cannot be observed. Regional differences are always apparent, due to various anatomical and physiological factors (Hardt and Hofer 1988). The main anatomical factor is the differing bone volume of each skeletal region. Uptake of the radionuclide is higher in bone of larger mass than in delicate bony structures. In the facial skeleton the uptake is slightly higher in the maxilla and mandible compared with the rest of the skull. The predominant physiological factors are local tissue perfusion and regional metabolic activity. In the growing skeleton the epiphyseal plates typically show increased activity.

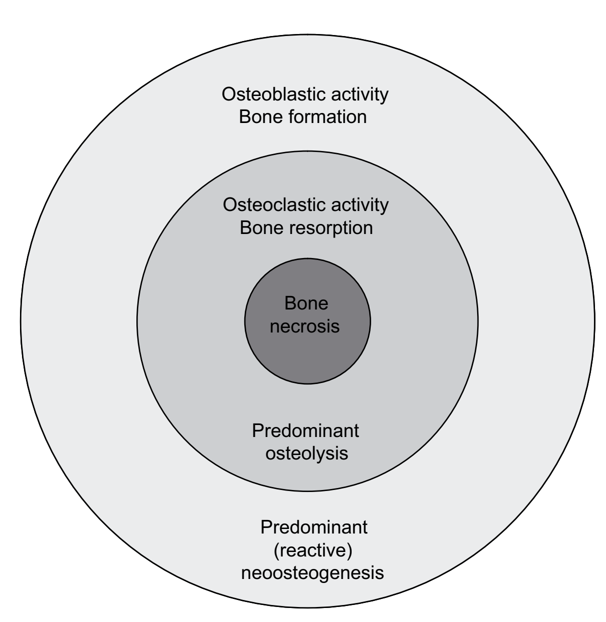


Fig. 4.2 Pathological–anatomical changes of bone tissue osteomyelitis of the jaws (Adapted from Hardt 2000, 2003)

Summarized when interpreting a bone scan, the following criteria must always be addressed:

- Look for symmetrical uptake within the corresponding skeletal regions
- Regions with increased or decreased uptake compared with surrounding and corresponding bones are suspicious and may need further radiological investigation
- Increased uptake is a sign of increased metabolic activity
- A physiological or decreased uptake indicates a normal osteoblastic bone activity or may be the result of a very aggressive lesion with failure of local bone repair

Pathological bone conditions can lead to alterations in local blood flow and induce bone metabolism causing an either increased resorption (osteolysis) or osteoblastic activity (sclerosis, periosteal reaction; Hardt and Hofer 1988).

As long as the vascular supply to the center and peripheral aspects of the bone lesion is maintained, an increased uptake is noted on the bone scan (Figs. 4.3, 4.4); however, if loss of bone is not repaired adequately, or local blood supply is compromised, the scintigraphic image will show a decreased uptake. The uptake within the center or the periphery of an osteolytic lesion on a radiograph therefore describes the osteogenic potency of the lesion or the degree of osteogenic repair mechanisms and indirectly the activity (Hardt and Hofer 1988; Handmaker and Leonards 1976; Hofer and Hardt 1983; Hofer et al. 1985).

An increased pathological uptake of radioactive tracer is noted in lesions which produce bone tissue, such as certain tumors, and, on the other hand, by processes which induce reparative bone reactions in the periphery of the lesion; examples for the latter are osteolytic metastasis.

A decreased uptake is noted in lesions which eventually replace bony matrix without any or little repair. This can be observed in slow-growing pathologies such as cysts or odontogenic tumors. Bone repair also depends on the aggressiveness of the lesion. In extremely fast and destructive growing tumors there is an almost complete breakdown of osteogenic repair.

4.5 Bone Scintigraphy in Osteomyelitis of the Jaws

4.5.1 General Aspects of Bone Scans in Osteomyelitis of the Jaws

The correlation of bone scans with the corresponding radiograph gives reliable information on the aggressiveness of a bone lesion. Bone scans are especially valuable when conventional radiographs or CT scans demonstrate a high level of activity with a mixed pattern of osteolysis and sclerosis or in cases where the clinical course of the disease leads to the assumption of an underlying aggressive pathology (Hardt and Hofer 1988; Hofer et al. 1983).

Compared with conventional radiographs, the following additional information can be gathered with bone scintigraphy (Hardt and Hofer 1988; Hardt 2000, 2003):

- Information is obtained from the whole skeleton.
- Scintigraphy is positive as soon as regional osteoblastic activity is increased. The latency period compared with conventional imaging is therefore reduced (Figs. 4.5, 4.6).
- Because osteoblastic activity is detected much earlier in bone scans, the dimension of the lesion can be determined more accurately (Figs. 4.6–4.17).
- The additional information on the activity in bone scans is, however, usually very unspecific with a widespread differential diagnosis.

Radionuclide is concentrated in all areas of the body with increased blood flow and osteoblastic activity. Since the whole body is included in the scanning process, still clinically silent lesions may be detected at an early stage. This can be important in metastatic spread hematogenous osteomyelitis or in cases of syndrome-associated primary chronic osteomyelitis (e.g., SAPHO syndrome or chronic recurrent multifocal osteomyelitis with involvement of the jaw).

Approximately one third to half of the bone mineral must be altered before changes are observed on conventional radiographs. These changes usually require at least 10–14 days or even longer after onset of the infection. In a study of 18 patients, conventional radiographs were definitely diagnostic of osteomyelitis in all patients only after 4 weeks (Schuknecht et al. 1997). Since radiopharmaceuticals in bone scans give particularly useful information on osteoblastic bone activities, rather than demineralization, changes may be seen as early as 3 days after onset of symptoms of osteomyelitis (Topazian 2002). This allows diagnosis of the disease in an early stage. Especially diagnosis of acute osteomyelitis may be facilitated with this tool and therapeutic intervention can be addressed before further progression to a chronic stage is established.



Fig. 4.3 Odontogenic secondary chronic osteomyelitis (axial CT view). The affected bone shows osteolysis, sclerosis, sequester formation, and a strong buccal and lingual periosteal reaction. The strong reactive bone formation noted in the CT scan is also demonstrated by a markedly increase of activity in the bone scan (hot spot)

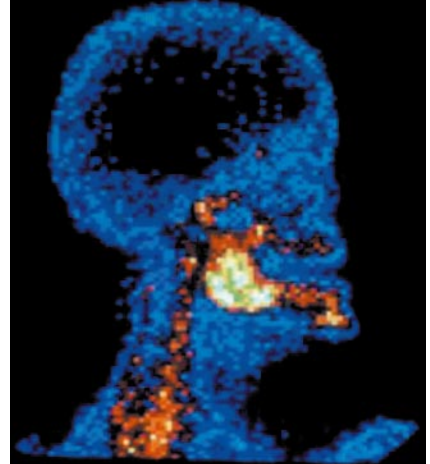


Fig. 4.4 Corresponding bone scan of Fig. 4.3

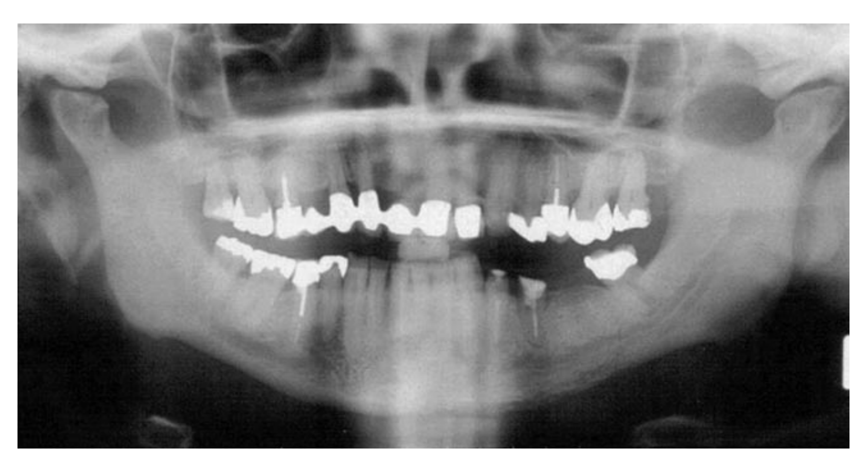


Fig. 4.5 Adult-onset primary chronic osteomyelitis with insinuating osteolysis in the symphyseal area



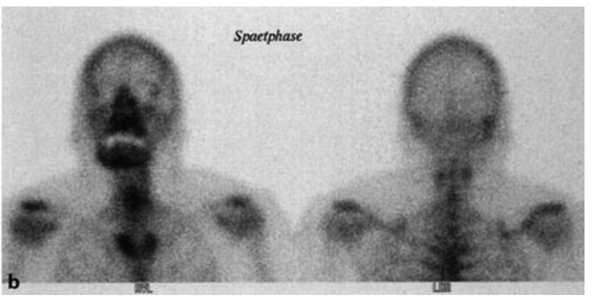


Fig. 4.6a,b Bone scans correspond to Fig. 4.5. An increased uptake is noted in the entire symphysis as well in anterior portion of right mandibular corpus



Fig. 4.7 Odontogenic secondary chronic osteomyelitis. The orthopantomography shows unclear demarked osteolysis of the left mandibular body and ascending ramus



Fig. 4.8 Bone scan corresponds to Fig. 4.7. The bone scans show an increased uptake of radionuclide in the whole left mandibular body from the condyle to the symphysis, and even part of the right mandibular body is affected. Compared with the orthopantomography Fig. 4.7 and the CT scans Figs. 4.10, 4.11, a clearly increased region shows signs of inflammation



Fig. 4.9 Bone scan corresponds to Fig. 4.7. The bone scans show an increased uptake of radionuclide in the whole left mandibular body from the condyle to the symphysis, and even part of the right mandibular body is affected. Compared with the orthopantomography Fig. 4.7 and the CT scans Figs. 4.10, 4.11, a clearly increased region shows signs of inflammation

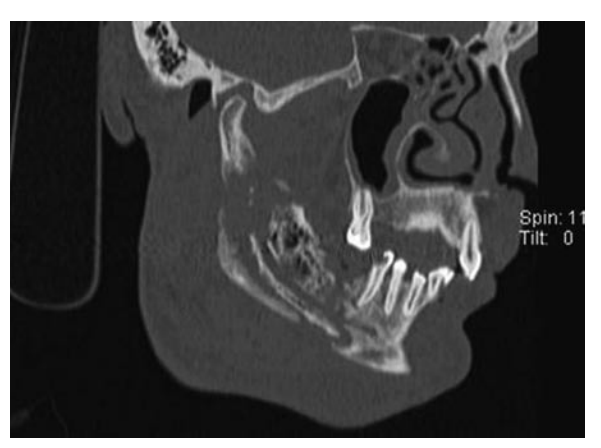


Fig. 4.11 Corresponding computed tomography scans in sagittal view of Fig. 4.7 (same legend as Fig. 4.10)



Fig. 4.10 Corresponding computed tomography scans in axial view of Fig. 4.7. The CT scan shows the affected area in more detail with marked osteolysis and destruction of the cortical bone and sequester formation in the body and ascending ramus of the left mandible

Because bone scans detect osteomyelitic lesions much earlier than conventional radiological imaging, the true dimension of the pathology is presented more accurately; hence, while in conventional imaging studies the lesion will be limited to the zone with significant osteolysis and osteosclerosis, the bone scan will be positive in larger areas. The sensitivity of bone scans also gives valuable additional information in monitoring cases of primary and secondary chronic osteomyelitis when a decision must be made regarding the need and extent of additional surgery or the duration of antibiotic therapy. It must be taken in account, however, that activity in bone scans usually ceases several weeks after inflammation subsides.

Bone scan can be generally described as a diagnostic tool with great sensitivity; however, these investigations lack specificity. Positive bone scans may be obtained in cases of infection, trauma, tumor, or degenerative lesions (Heuck and Zum Winkel 1980). To further narrow differential diagnosis other imaging studies are necessary (Hardt and Hofer 1988), and biopsy procedures are sometimes unavoidable to secure diagnosis.

4.5.2 Indications for Bone Scans of the Facial Skeleton in Osteomyelitis Cases

The advances in diagnostic imaging, especially high-resolution CT and MRI, have proven a significant increase in sensitivity compared with conventional imaging. The above-mentioned disadvantages of conventional radiographs compared with bone scans have partially been overcome with these imaging techniques. These developments have somewhat reduced the need for scintigraphic studies. In certain indications, however, bone scans are still considered to be a valuable enrichment to the armamentarium of diagnostic studies. Especially the use of combined imaging studies in the past 2 decades, using bone scan technology and CT has demonstrated advantages compared with each technology on its own.



Fig. 4.12 Early-onset primary chronic osteomyelitis. The orthopantomography shows a significant sclerosis and some osteolysis of the ascending ramus on the right side.



Fig. 4.13 Corresponding computed tomography scans of Fig. 4.12 in axial views. A much clearer picture is given in the axial CT scans with a predominant sclerosis and some osteolysis with a marked periosteal reaction of the mandibular angle and the ascending ramus



Fig. 4.14 Corresponding computed tomography scans of Fig. 4.12 in axial views. A much clearer picture is given in the axial CT scans with a predominant sclerosis and some osteolysis with a marked periosteal reaction of the mandibular angle and the ascending ramus



Fig. 4.15 Corresponding computed tomography scans of Fig. 4.12 in axial views. A much clearer picture is given in the axial CT scans with a predominant sclerosis and some osteolysis with a marked periosteal reaction of the mandibular angle and the ascending ramus

This combined imaging study, also known as single photon emission computed tomography (SPECT), provides three-dimensional imaging that is more useful in detecting small lesions. Hakim and coworkers (2006) concluded, in a study of 42 patients with osteomyelitis of the jaws, that SPECT was vastly superior to other diagnostic methods in initiating treatment, mainly due to its high sensitivity.

Every skeletal disease may be considered an indication for a bone scan. To achieve the maximum benefit of a diagnostic tool, it is important to reconsider every indication before administering them. Bone scans should only be obtained if they facilitate diagnosis and replace other more invasive or more expensive diagnostic studies (Hardt and Hofer 1988; Hardt 2000, 2003; Bessler 1985). As with all diagnostic imaging studies major and relative indications are distinguished. The following indications represent the ones still commonly used in most maxillofacial units:

- Early diagnosis of osteomyelitis, especially with other negative imaging studies and a highly suspected clinic
- Evaluation of the activity of a lesion
- Determining accurate distribution of the infection locally as well as detecting additional infectious lesions of the skeleton
- Monitoring of the infection using comparative activity studies to determine effectiveness of antibiotic and/or surgical therapy, especially in cases where radiological images still demonstrate residual sclerosis (Hardt and Hofer 1988)

4.5.3 Early Diagnosis of Osteomyelitis of the Jaws

Every pathological process in the bone can alter local perfusion or bone metabolism and therefore lead to a positive scintigraphic result. As mentioned previously, ^{99m}Tc-labled methylene diphosphonate is the standard radiopharmaceutical in use for tracing bone activities and hence also the primary choice in bone scan of suspected osteomyelitis cases (Jones and Cady 1981; Hardt et al. 1984; Hardt 1991; Burkhart 1995). Bone infections appear positive in bone scans as soon as reactive osteogenesis has developed a sufficient measurable intensity (Hardt 1991; Bergstedt and Lind 1978). Markedly increased bone turnover activity as indicated by scintigraphy has been reported as an early sign in acute osteomyelitis (Rohlin 1993; Köhnlein et al. 1997).

A positive scan can be found in acute osteomyelitis as early as 24–48 h after onset of clinical symptoms due to hyperemia, although in most instances it does take up to 3 weeks until the result is clearly positive (Mercuri 1991; Hardt and Hofer 1988; Reinert et al. 1995). The degree of uptake was reported as higher when plain films showed permeative bone destruction and areas of osteolysis compared with the moth-eaten or sclerotic appearance that prevails in chronic osteomyelitis (Rohlin 1993). With histology as reference, the sensitivity in the acute phase is postulated to be close to 100%, and false-negative results are attributed to the fact that the examination has been performed too early (Köhnlein et al. 1997). Also in cases of highly aggressive spread of the disease, the uptake of tracer substance may be diminished and the bone scan false negative. This is explained by the increased intramedullary pressure due to the infection, jeopardizing vascular supply. Scintigraphic examinations turn positive after the intramedullary pressure has been decreased and uptake of tracer is again possible. This is usually the case after a period of 4–6 days. If earlier diagnosis is attempted, MRI investigations should be conducted because of their well-known advantages compared with bone scans at this stage of the disease (Köhnlein et al. 1997; Körner et al. 1997).

Acute osteomyelitis as well as cases of primary chronic osteomyelitis may produce similar results in scintigraphic images at an early stage. Differentiation of these two disease entities must be made using further radiological investigation and by observing the clinical course (Hardt 2000, 2003; Scharf et al. 1978).

Further drawbacks of scintigraphy in acute osteomyelitis are related to the fact that distinction between soft tissue inflammation and bone involvement is limited (Tsuchimochi et al. 1991; Rohlin 1993); therefore, as a preoperative examination, scintigraphy is not sufficient to determine the extent of mandibular osteomyelitis. It must be complemented by an additional CT examination to provide detailed information (Schuknecht et al. 1997; Heggie 2000).

In conclusion, it can be stated that due to its high sensitivity and relatively low cost, bone scans can still be considered as a primary investigation tool in suspected cases of acute osteomyelitis or early stages primary chronic osteomyelitis; however, the above-stated advantages and increased availability have somewhat led to a replacement of bone scans by MRI investigations in the early diagnosis of acute and primary chronic osteomyelitis of the jaws.

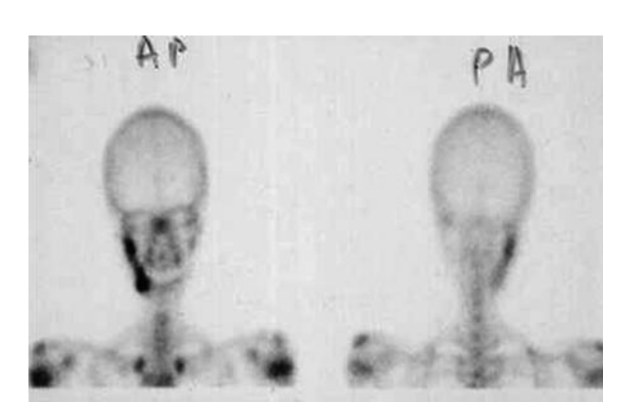


Fig. 4.16 Corresponding bone scans of Fig. 4.12. The bone scans reveal a somewhat extended reactive bone with increased uptake within the entire right angle and ascending ramus up the mandibular collum

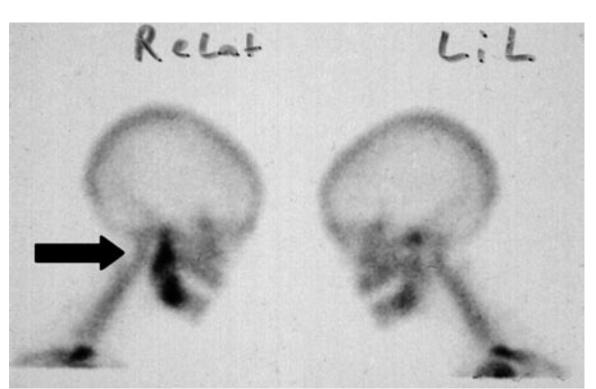


Fig. 4.17 Corresponding bone scans of Fig. 4.12. The bone scans reveal a somewhat extended reactive bone with increased uptake within the entire right angle and ascending ramus up the mandibular collum (*arrow*)

4.5.4 Disease Activity

The uptake of radionuclide tracer substance within an infectious bone lesion is proportional to the amount of bone repair and therefore indirectly gives information on the activity of the process. According to Gates (1980) bone scans in mandibular osteomyelitis are positive in 95% of cases. When a localized osteitis, as commonly noted in periapical infections or after third-molar surgery, is sequenced by osteomyelitis, corresponding to deep bone invasion of the infection, bone scans show a clearly increased distribution of activity. This fact is useful to distinguish simple periapical pathologies or delayed healing of an extraction alveole from osteomyelitis at an early stage when conventional radiology fails adequate detection (Figs. 4.18–4.20).

In patients with acute and secondary osteomyelitis, as well as in primary chronic osteomyelitis of the jaws, the uptake of tracer is increased. This is also the case in osteomyelitis with negative radiographs due to early administration of antibiotics. Especially in cases of secondary chronic osteomyelitis with a predominant sclerosing radiographic appearance bone repair mechanisms clearly mask necrosis and resorption. The registered activity of these cases is mostly higher than seen in malignant bone tumors but lower than in tumor-like lesions such as fibrous dysplasia.

Although bone scanning does give certain clues helpful for making differential diagnosis, it must be clearly stated that scintigraphy by its self cannot be used to differentiate osteomyelitis from aggressive bone malignancies or to distinguish various types of osteomyelitis (Hardt 2000, 2003; Hofer and Hardt 1983; Hardt 1991; Gates 1980).

Necrotic areas of bone also lead to an increased turnover of bone tissue in their periphery, demonstrating a positive bone scan of these regions. In rare instances infections resulting from a venous thrombosis may lead to a complete breakdown of tissue perfusion in the infected area. Radioactive tracer cannot reach the site of infection any closer. In cases of highly acute jaw osteomyelitis bone scans may therefore be negative in the affected area (Hardt and Hofer 1988; Handmaker and Leonards 1976; Hofer and Hardt 1983).

4.5.5 Determining the Extent of a Lesion in Osteomyelitis

The infectious lesion in osteomyelitis always demonstrates a larger extent in bone scans compared with the osteolytic area in conventional imaging (Hardt et al. 1986). The full extent of a lesion cannot be determined in conventional radiographs. Due to their increased sensitivity, bone scans allow definition of the true extent of an infectious bone lesion far more accurately. The extent of the process, especially in chronic courses, is determined with the same precision as MRI scans and hence bone scans are even more accurate than high-resolution CT scans with a fraction of the administered radiation (Figs. 4.21–4.28).

The appearance of multiple-spread osteomyelitis lesions throughout the entire skeleton is noted mostly in young infants and small children. In this age group



Fig. 4.18 Odontogenic secondary chronic osteomyelitis after surgical removal of the left lower third molar: orthopantomography shows an empty alveolus with somewhat extended osteolysis

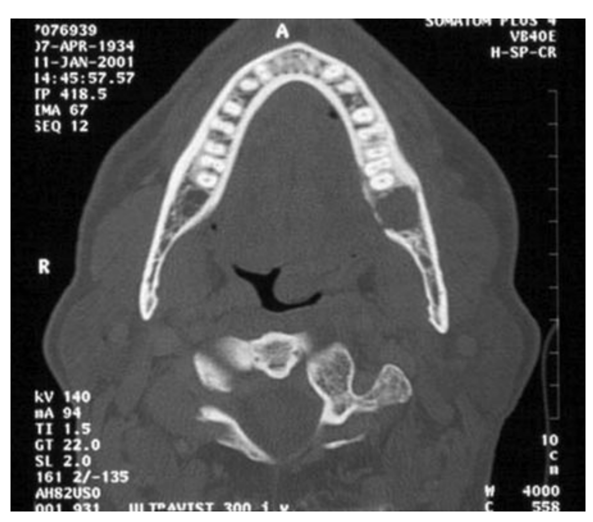


Fig. 4.19 The CT scan (axial view; same patient as in Fig. 4.18) reveals further destruction of the lingual cortical bone



Fig. 4.20 The bone scan (same patient as in Fig. 4.18) reveals massively increased uptake in the affected region corresponding to a highly active local metabolic turnover of bone. The affected area is clearly larger than on the conventional radiographs and the CT scan shown in Figs. 4.18 and 4.19



Fig. 4.21 Odontogenic secondary chronic osteomyelitis. The CT scan demonstrates localized osteolysis in the anterior left mandible with sequester formation and reactive perifocal sclerosis which extends to the symphysis to the anterior and to the mandibular body distally

bone scans are indicated to determine all sites of infection and to detect possible clinically silent lesions. Also in cases of syndrome-associated primary chronic osteomyelitis (e.g., SAPHO syndrome and chronic recurrent multifocal osteomyelitis (CRMO) with involvement of the jaw) scintigraphic investigation is advantageous for the same reason (Fig. 4.29).

4.5.6 Monitoring the Course of Osteomyelitis

Since scintigraphic bone scans can determine the exact extent of an osteomyelitis lesion, it is also a suitable tool for monitoring the disease; however, to obtain conclusive results, a series of bone scans are necessary during the course of the disease (Hardt 2000, 2003; Burkhart 1995). Based on clinical data and the administered therapy, a follow-up bone scan should already

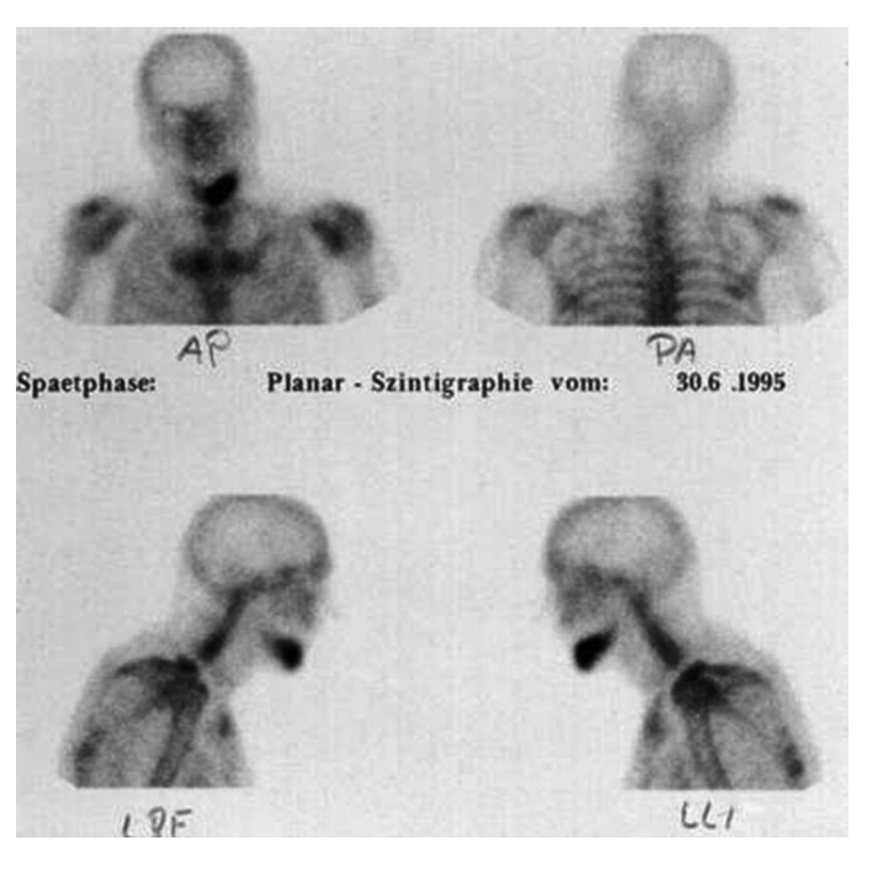


Fig. 4.22 The corresponding bone scan (same patient as in Fig. 4.21) shows a somewhat more distinct and extensive lesion than the CT scan with inflammatory activity reaching distally to the mandibular angle

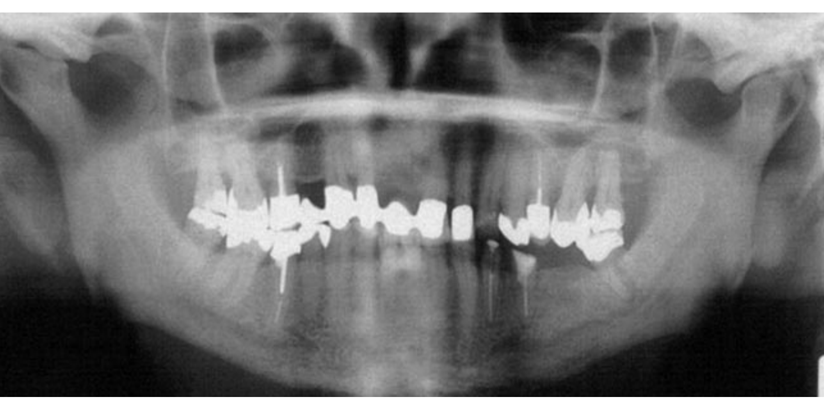


Fig. 4.23 Adult-onset primary chronic osteomyelitis of the mandible: orthopantomography with discrete sclerosis in the symphysis area and anterior right and left body of the mandible

Fig. 4.24 The corresponding axial CT scan (same patient as in Fig. 4.23) shows a more distinct pattern with sclerosis and osteolysis and cortical defects of the entire right mandibular body as well the left anterior mandible



Fig. 4.25 The corresponding axial CT scan (same patient as in Fig. 4.23) shows a more distinct pattern with sclerosis and osteolysis and cortical defects of the entire right mandibular body as well the left anterior mandible



Fig. 4.26 The corresponding MRI (same patient as in Fig. 4.23) demonstrates a hypointense bone marrow in the symphysis and the anterior mandibular body on both sides as a sign of marrow fibrosis/sclerosis

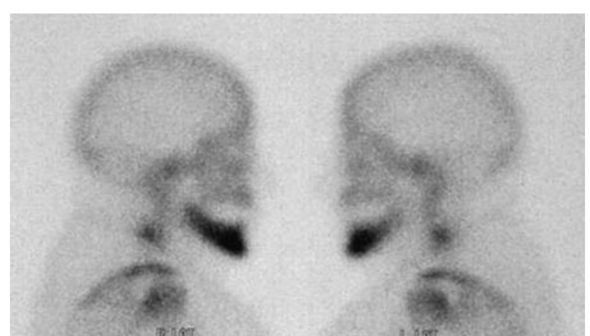


Fig. 4.27 The corresponding bone scans (same patient as in Fig. 4.23) shows an increased uptake of radionuclide in the right mandibular body and parts of the ascending ramus as well the anterior part of the left mandibular body

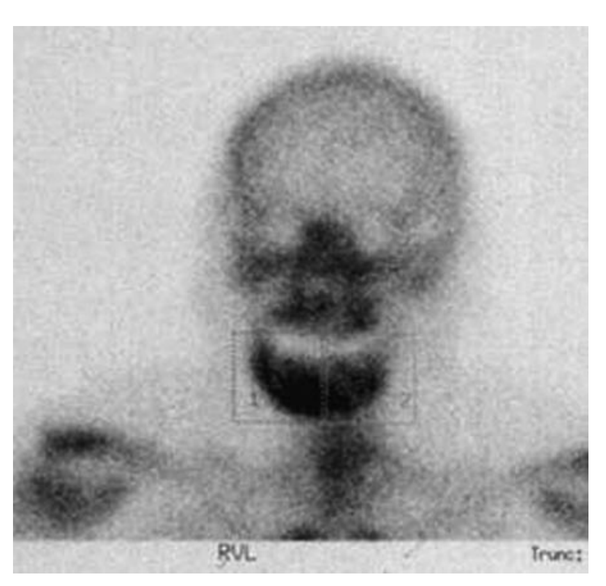


Fig. 4.28 The corresponding bone scans (same patient as in Fig. 4.23) shows an increased uptake of radionuclide in the right mandibular body and parts of the ascending ramus as well the anterior part of the left mandibular body

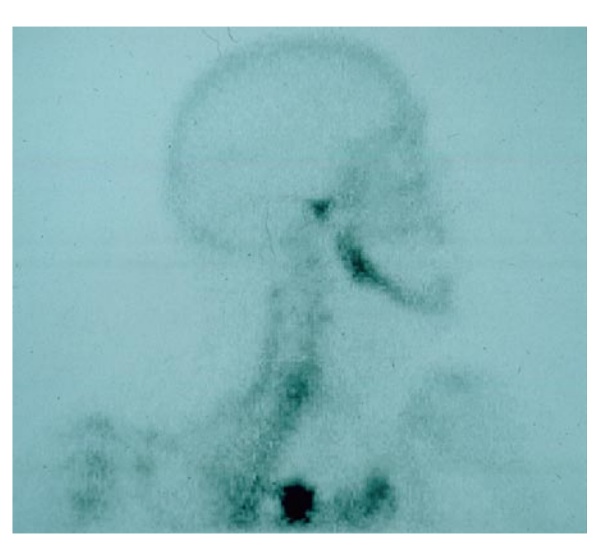


Fig. 4.29 Patient with adult-onset/syndrome-associated primary chronic osteomyelitis. The scintigraphic imaging demonstrates a significant enhancement of the right mandibular body and the left sterno-clavicular joint. (This case is described in detail in Chap. 12, case report 15)



Fig. 4.30 Early-onset primary chronic osteomyelitis: orthopantomography

be planned at first presentation and an initial scan ideally obtained to register baseline activity before starting treatment.

After surgical removal of the infected and necrotic bone tissue, the activity in postoperative bone scans is increased. This is explained by intensive remodeling process and repair mechanisms which are to be interpreted as a physiological response of the bone. In analogy to fracture healing a postoperative bone scan remains positive for several weeks and should not be misinterpreted as a relapse of infection. Usually after a period of 2–4 months uptake values of radioactive tracer slowly decrease and eventually turn to normal levels providing complete cure (Figs. 4.30–4.39).

In cases of relapse of osteomyelitis, or failure to fully eradicate the infection due to inadequate therapy, a gradual increase in scintigraphic activity is usually noted. This fact allows facilitating the decision whether an additional surgical procedure or other therapeutic modalities, such as prolonged antibiotics or HBO, should be administered.

If surgery consists of immediate replacement of the resected bone with a transplant, as described by Obwegeser (1960), Obwegeser and Sailer (1978), and Sailer



Fig. 4.31 Corresponding CT scan (same patient as Fig. 4.30) at first presentation demonstrates diffuse sclerosis of the left mandible and thickening of the cortical bone in the affected area. Some osteolysis are further notable in the CT scans

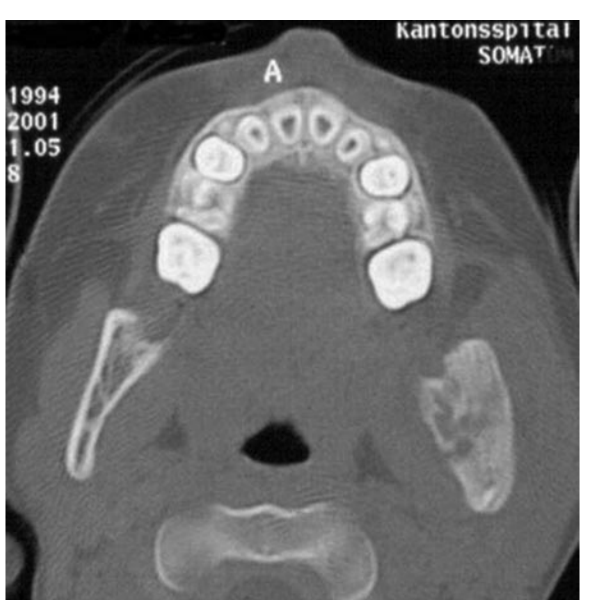


Fig. 4.32 Corresponding CT scan (same patient as Fig. 4.30) at first presentation demonstrates diffuse sclerosis of the left mandible and thickening of the cortical bone in the affected area. Some osteolysis are further notable in the CT scans



Fig. 4.33 The corresponding bone scan (same patient as Fig. 4.30) shows an increased uptake in the angle and ascending ramus of the left mandible



Fig. 4.34 The corresponding bone scan (same patient as Fig. 4.30) shows an increased uptake in the angle and ascending ramus of the left mandible

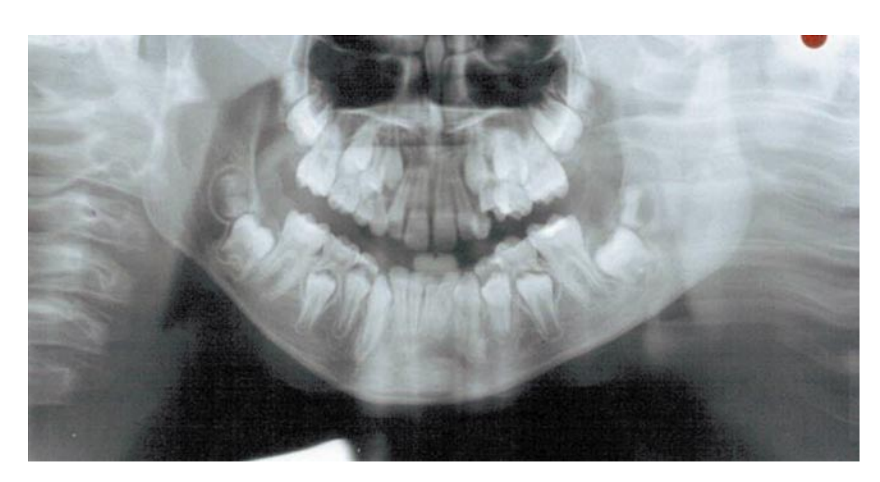


Fig. 4.35 Same patient as in Figs. 4.30–4.34, 20 months later, after hyperbaric oxygen and prolonged antibiotic therapy. The orthopantomography and anteroposterior film show a persistent homogenous sclerosis of the left angle and ascending ramus. The increased bone volume remains more or less unchanged, but the osteolysis has disappeared



Fig. 4.36 Same patient as in Figs. 4.30–4.34, 20 months later, after hyperbaric oxygen and prolonged antibiotic therapy. The orthopantomography and anteroposterior film show a persistent homogenous sclerosis of the left angle and ascending ramus. The increased bone volume remains more or less unchanged, but the osteolysis has disappeared

(1984), bone scans are useful to monitor activity around and within the transplant and hence give valuable information on the biological success of the transplantation (Ewers et al. 1978).

Healed osteomyelitis often leaves a region of increased sclerosis behind. This can be observed in radiographs and is referred to as bone scar. In bone scans these "scars" tend to show a physiological to slightly increased activity.

4.5.7 Additional Scintigraphic Bone Scans

As mentioned previously, ^{99m}Tc-labeled methylene diphosphonate is the most common radiopharmaceutical used in performing scans for osteomyelitis. Addition of a ^{67}Ga study to the ^{99m}Tc scan can aid in distinguishing osteomyelitis from malignancy and trauma. Since gallium imaging is one of the most sensitive and specific radionuclide scanning technique for osteomyelitis, positive findings on both scans usually confirm the infectious nature of the disease. When the ^{99m}Tc-scan result is positive and the ^{67}Ga scan is negative, osteomyelitis may not be the primary disease. Gallium-67 uptake that exceeds ^{99m}Tc uptake indicates acute inflammatory disease. In primary and secondary chronic osteomyelitis reduced activity in follow-up ^{67}Ga scans is a useful indicator for termination of therapy in osteomyelitis. Indium-111 in leucocyte scintigraphy may also be useful in determining when a lesion is inactive and therapy may cease. As a follow-up examination, simultaneous indium-111 WBC/Tc-99m-MDP bone SPECT scintigraphy has been found to revert back to normal after successful treatment much sooner than CT (Weber et al. 1995).



Fig. 4.37 The corresponding CT scan (same patient as in Fig. 4.35) shows a persistent homogenous sclerosis of the left angle and ascending ramus. The increased bone volume remains more or less unchanged, but the osteolysis has disappeared



Fig. 4.38 The corresponding CT scan (same patient as in Fig. 4.35) shows a persistent homogenous sclerosis of the left angle and ascending ramus. The increased bone volume remains more or less unchanged, but the osteolysis has disappeared

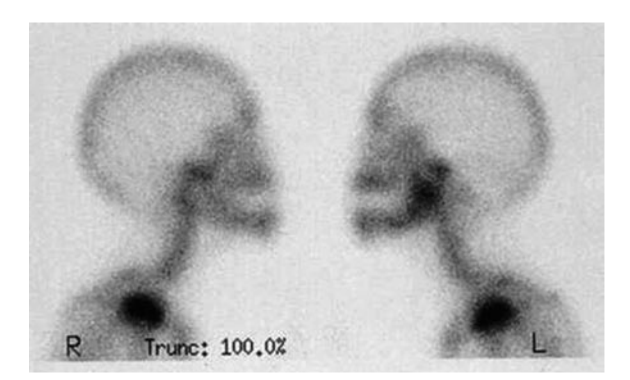


Fig. 4.39 Corresponding CT scan of Fig. 4.35. A significant decrease in activity of the bone scans demonstrates a decrease of disease activity which corresponds to a reduction of clinical symptoms

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Diagnostic Imaging – Positron Emission Tomography, Combined PET/CT Imaging

Andrej Terzić and Gerhard Goerres

5

Contents

5.1 Summary

Positron emission tomography (PET) is a relatively new non-invasive technique to investigate various bone and soft tissue pathologies. The combination of PET scanners and radioactive tracing substances, nowadays most commonly fluorine-18-fluoro-2-deoxy-D-glucose (^{18}FDG), provides three-dimensional images in very short time depicting biological activity rather than anatomy; however, ^{18}FDG does not only accumulate in osteomyelitis of the jaws but also in many other conditions such as fractures, malignant tumors, and in sterile and non-sterile inflammations. Both accurate knowledge of concomitant diseases and therefore careful indication minimize false-positive results and guarantee high specificity and a good positive predictive value.

The use of PET in osteomyelitis of the jaws has only been investigated recently and published data is very scarce. The development of fused PET/CT images is particularly promising since it combines the advantages of a detailed imaging of the anatomy combined with detection of local metabolic activity pattern; hence, for the first time, this technique offers simultaneously direct information of form and function of bone pathology.

High costs and limited availability are the major drawbacks for PET and fused PET/CT investigation; however, as technology advances this imaging tool will inevitably become more widely used and experience will increase, making it a very promising diagnostic tool for assessment of osteomyelitis in the future.

5.2 General Aspects of Positron Emission Tomography

In general, plain radiographs are usually the first radiological investigations performed when suspicious of jawbone osteomyelitis. They are inexpensive and easy to obtain but are not unambiguous; thus, magnetic resonance imaging (MRI), computed tomography (CT), and in some instances scintigraphy, may be necessary to confirm diagnosis, determine extents of the lesion and plan adequate therapy. Histology, which is considered a secondary diagnostic criterion (see Table 2.7. Chapter 2), is useful to confirm the diagnosis and to rule out other pathologies in unclear cases. Indeed, untypical cases, especially primary chronic osteomyelitis of the jaws, can be a demanding challenge (in some instances impossible) to diagnose with non-invasive methods alone.

Positron emission tomography (PET), also called PET imaging or PET scanning, has recently been shown to be a promising non-invasive tool for accurate diagnosis of various bone pathologies. It was first introduced in the early 1970s. During investigation the patient is administered a radioactive substance and the subsequently emitted radiation is recorded by a scanner resulting in a three-dimensional image of the body. In contrast to

other radiological exams, such as CT or MRI scans, PET does not show an anatomical reproduction but a map of the metabolic activity depending on the distribution of the radioactive substance. It reflects the biochemical pattern in different body tissues and can give images of single organs, but also of various parts of the body or the entire body.

In the late 1990s the fusion of simultaneously acquired CT and PET scans (PET/CT) allowed the three-dimensional depiction of anatomy and the uptake of the nuclide at the same time contributing to more precise localization of diseased tissue. PET underwent a fast development in the following years and since the 1990s it is in regular clinical use to determine head and neck pathology, especially in cancer-related patients (Alavi 2004). It is also useful in diagnosing certain cardiovascular and neurological diseases, because it shows areas with increased, diminished, or no metabolic activity. In recent years its value for non-invasive detection and follow-up of inflammatory conditions was increasingly investigated, and there is evidence for early detection of different acute infections (Sugawara et al. 1998). A recent meta-analysis describes PET in combination with the radioactive tracer fluorine-18-fluoro-2-deoxy-D-glucose (^{18}FDG) as the safest non-invasive method to detect chronic osteomyelitis with a sensitivity of 96% and specificity of 91% (Termaat et al. 2005), and it is judged to be better for diagnosing chronic osteomyelitis than bone/leucocyte scan (Guhlmann et al. 1998b). Furthermore, it is useful in monitoring the response after non-surgical treatment (Kallicke et al. 2000; Sugawara et al. 1998).

Due to its high purchasing costs and high expenses for maintaining a complete service, presently the availability of PET is the limiting factor for the day-to-day application (Crymes et al. 2004). Apart from this, the actual cost-effectiveness has not yet been given (Schirrmeister et al. 1999), and in most countries it is not reimbursed by insurance companies. Until it becomes more available in daily use, it has to be considered a very promising investigation technique of the future in detecting both primary and secondary osteomyelitis, possibly showing more reliable results than any other conventional, non-invasive method.

5.3 Fluorine-18-fluoro-2-deoxy-D-glucose PET

There is an abundance of imaging agents in nuclear medicine. In combination with PET, a certain number of mainly short-lived positron-emitting radionuclides, such as ^{11}C, ^{13}N, ^{15}O and ^{18}F, must be mentioned. Presently, the most frequently used radioactive tracer in PET is fluorine-18-fluoro-2-deoxy-D-glucose (^{18}FDG). Its radioactive component is the 18-F fluoride, a positron-emitting radionuclide. It is very short-lived with a half-life of 110 min, allowing minimal radioactive exposure to the patient. The applied dose of 0.027 mSv/MBq (Millisievert per Megabecquerel) is dose equivalent to a conventional CT scan (De Winter 2002 et al.), and it can be considered a safe tracer, since no negative side effects of ^{18}FDG have been reported so far. While it can take weeks until there is evidence of disease on a plain radiograph (Tememrmann et al. 2001), bone scans with radionuclides turn positive at a much earlier stage of the disease (see also Chap. 4 Scintigraphy Scintigraphy). Another advantage of ^{18}FDG is the short time to accumulate in the tissue of interest. ^{18}FDG PET scans detecting osteomyelitis are ready for interpretation as soon as 1 h after injection. They have a high early target-to-background ratio compared with the 4- to 24-h latency in conventional scintigraphy or scintigraphy with radionuclide-marked white blood cells (WBC scintigraphy; Sugawara et al. 1998).

On the other hand, the quick decay of ^{18}FDG poses serious logistical problems. There is a need for a nearby-located laboratory producing the tracer which guarantees the accurately timed availability of ^{18}FDG before the tracer is decayed. Once injected in the blood, ^{18}FDG passes through the cell membrane as a glucose analog by carrier-mediated transport. In tumor patients the process of accumulation in diseased tissue is well investigated and described (Pauwels et al. 2000). In inflammation accumulation of ^{18}FDG was reported in both aseptic and bacterial infections (Yamada et al. 1995; Sugawara et al. 1998), but the uptake is not completely understood; however, it seems to be linked to the elevated glucose influx as an energy source for leukocytes and macrophages when they are metabolically active in inflamed tissue (De Winter et al. 2002; Kaim et al. 2002). At the same time, inactivated white blood cells in other sites show only a weak uptake (Stumpe et al. 2000). Finally located in the inflamed tissue, ^{18}FDG emits a positron which annihilates with an electron thereby producing a pair of photons aiming in nearly opposite directions. Afterward, the two emitted high-energy gamma rays (511 keV) are detected by PET scanners placed exactly 180° opposite each other. They must arrive at the scanners in full chronological coincidence to be registered. As a result the amount of activity allows the computer to reassemble the signals into three-dimensional images. On the final PET images the spatial distribution

of FDG and the amount of radiotracer activity can be identified allowing for quantification of tracer uptake in a region of interest.

5.4 Clinical Possibilities and Limitations of ^{18}FDG PET

In almost all pathological conditions there is increased metabolic activity with simultaneously increased accumulation of ^{18}FDG. Up-to-date ^{18}FDG uptake was reported in a wide variety of diseases including fractures (Ravenel et al. 2004; Meyer et al. 1994) and malignant tumors (Schmid et al. 2003; Goerres et al. 2002). There is also evidence for accumulation in sterile inflammations such as sarcoid lesions (Lewis and Salama 1994), inflammation of the airways in allergic asthma (Taylor et al. 1996), SAPHO syndrome (Kohlfuerst et al. 2003; Pichler et al. 2003) and turpentine-induced inflammation in rats (Yamada et al. 1995). Regarding bacterial infections, an elevated uptake was noted in osteomyelitis (Hakim et al. 2006; Sugawara et al. 1998) as well as in cases of cellulitis and abscess formation (Sugawara et al. 1998). So it is easy to understand that PET is not able to differentiate between simultaneously appearing diseases; hence, positive PET scans are not specific for osteomyelitis but can also depict concomitant diseases such as the aforementioned. Illuminating the general medical history of the patient possibly undergoing PET is hence of crucial importance, and pre-existing conditions with an elevated ^{18}FDG uptake must be considered a relative contraindication for PET in cases of suspected osteomyelitis. In detail, PET is of limited value applied for discrimination between malignant or inflammatory processes, because both conditions have a high ^{18}FDG uptake (Guhlmann et al. 1998a; Love et al. 2005). For the same reason it is difficult to differentiate between metastasis and infection in patients with malignant tumors (Kallicke et al. 2000) as well as primary bone tumors and osteomyelitis (Guhlmann et al. 1998a). Some approaches for better discrimination by applying dual time scans are not well validated (Hustinx et al. 1999).

Thus far, very little has been published concerning the natural history of FDG accumulated in fractures. As mentioned, ^{18}FDG uptake in fresh fractures is high (Ravenel et al. 2004; Meyer et al. 1994); thus, early PET after bone surgery may lead to false-positive results and mimic osteomyelitis (Koort et al. 2004). Reporting from general traumatology, Zhuang et al. (2003) recently found in a retrospective analysis of 37 patients that in acute fractures ^{18}FDG accumulates in the fracture zone due to activated inflammatory cells. Their data suggested that increased accumulation of ^{18}FDG for longer than 3 months after the trauma is to be linked with infection or malignancy rather than with trauma or surgery (Zhuang et al. 2003). Still, both the exact characteristics of ^{18}FDG concentration varying in different phases of infection as well as in which cells exactly the changes take place is not completely understood (Kaim et al. 2002). So it must be admitted that at present PET is of restricted use in postoperative situations (Love et al. 2005); however, possible benefit of PET at an early stage of infection was postulated in an animal experiment. Koort et al. (2004) created a localized osteomyelitis model in the tibia of rabbits and were able to distinguish between normal bone healing and bone infection. While normal healing was associated with a transient increased uptake of ^{18}FDG which tended to normalize within 6 weeks, inflamed bone showed an intense, continuous uptake of ^{18}FDG over the same period of time (Koort et al. 2004). It was moreover suggested that 3 months (Zhang et al. 2003) or possibly 3–6 months (De Winter et al. 2002) are needed to clearly avoid false-positive results in posttraumatic or postoperative situations due to non-specific uptake of the radionuclide.

Positron emission tomography unquestionably has numerous advantages to offer. There is a high lesion-to-background ratio which offers better detection than in conventional radiological methods (Stumpe et al. 2000; Meller et al. 2002). The resolution is in the millimetre range (Crymes et al. 2004) and provides high quality of spatial resolution (De Winter et al. 2002; Guhlmann et al. 1998b). It is better than in any other investigation in nuclear medicine (Stumpe et al. 2000; Meller et al. 2002) and other functional imaging techniques (Crymes et al. 2004). As the uptake of ^{18}FDG in normal bone is low (Crymes et al. 2004; De Winter et al. 2002; Stumpe et al. 2006) PET is an especially valuable tool for detecting small lesions in diseased bone. Compared with radionuclide bone scintigraphy (RNB scintigraphy), ^{18}FDG PET unravels very small lesions at an earlier stage (Kallicke et al. 2000). Furthermore, non-attenuation corrected PET is not disturbed or distorted in quality or resolution by any sort of implants (Guhlmann et al. 1998a; De Winter 2002). This clearly offers advantages compared with CT and MRI scans when investigating patients with extensive dental reconstructions. Moreover, the biomechanism in PET relying on metabolic activity allows distinguishing between a scar and active inflammation (De Winter et al. 2002). Inflamed soft tissue and inflamed bone in osteomyelitis can be separated easily (Guhlmann et al. 1998b; Kallicke et al. 2000; Keidar et

al. 2005). It is reported that there are no false-positive results for inflammation; thus, negative PET scans accurately exclude possible active inflammation with a high negative predictive value (Zhuang et al. 2000; De Winter et al. 2002).

As a recent technique some aspects in PET and inflammation are not elucidated. It is suggested that less uptake of ^{18}FDG allows differentiation of fractures and pseudarthrosis from inflammation (Kallicke et al. 2000), but there is no clinical importance yet. In the same way the correlation between ^{18}FDG uptake and influence of various bone sites, age of the patients (Zhuang et al. 2003) and possible different patterns of uptake for diverse bacteria remain unexplored (Koort et al. 2004).

5.5 ^{18}FDG PET in Osteomyelitis of the Jaws

Although the discussion of the application of PET in osteomyelitis is quite lively, exceptionally scarce information is available for the use of ^{18}FDG PET in cases of osteomyelitis of the jaws. The data are based on a handful of patients. Two patients are mentioned in general reports on osteomyelitis. One of them suffered from a secondary chronic osteomyelitis of the mandible (Guhlmann et al. 1998a) and one from a chronic paranasal sinusitis (Sugawara et al. 1998). Very recently the first report on osteomyelitis in head and neck and PET was published. Hakim et al. (2006) investigated the value of ^{18}FDG PET vs bone scintigraphy with ^{99m}Tc SPECT for primary diagnosis and follow-up in secondary chronic osteomyelitis of the mandible. Apart from ^{18}FDG PET and SPECT results they also collected laboratory parameters and clinical findings (not discussed in this chapter). The study included 42 patients preliminarily diagnosed with secondary chronic osteomyelitis of the mandible. In the first group 34 patients underwent PET and SPECT at the time of diagnosis. After surgical treatment, bone biopsy was available in 30 of the 34 patients. In the second group, in another 8 patients previously diagnosed with secondary chronic osteomyelitis 6 months earlier, PET and SPECT were performed during the follow-up period. Here histology was available in 6 patients who had to undergo revision. In both groups positive histology was considered the standard of reference for diagnosing osteomyelitis, regardless of scintigraphy or PET. The setting included monthly repetition of SPECT and PET in 1-month intervals resulting in totally 86 investigations. In comparison with histology, these investigations revealed 6 false-negative and 29 false-positive cases in scintigraphy, whereas PET showed 18 false-negative and 6 false-positive cases. Sensitivity and specificity were calculated. It was 88.2 and 17.1% in scintigraphy and 64.7 and 82.8% in ^{18}FDG PET, respectively. It is more rewarding to have a closer look at the initial investigations in group one without the follow-up considered for evaluation because this represents the everyday clinical situation in primary assessment of the disease. Sensitivity, specificity and positive predictive value were 84, 33.3 and 77% in scintigraphy, and 64, 77.7 and 88.8% in PET, respectively. There was non-significant correlation with secondary chronic osteomyelitis in scintigraphy and positive correlation in PET; thus, scintigraphy was better for initial true-positive findings, but ^{18}FDG PET was much better for true-negative findings. It is interesting to further illuminate the only two false-positive results in ^{18}FDG PET in this group because it emphasizes the fundamental importance of general medical history. One of the patients suffered from a pseudoarthrosis after fracture management, the other from a distant metastasis of a ductal carcinoma of the breast. As mentioned above, both diseases are relative contraindications in PET investigating inflammation. With the two patients excluded from the study the positive predictive value would have been very high; however, there is encouraging data concerning PET for early monitoring response after surgical intervention. Full information concerning PET, SPECT and clinical remission was available in 12 from 34 patients in the first group. While SPECT still showed active disease, ^{18}FDG PET was negative 1 month after surgery in 2 patients and 2 months after surgery in 5 patients, respectively. The same pattern was observed in another 2 patients after 5 and 7 months, respectively, whereas the remaining 3 patients showed incoherent findings regarding PET, SPECT and clinical remission. The importance herein lies in early negative ^{18}FDG PET allowing the cessation of concomitant antibiotic therapy.

Even if the results in this report do not confirm the generally good accuracy and predictive value for osteomyelitis in the mandible compared with the rest of the body, further studies must be done. Without a doubt, more data are needed to clearly elucidate the factors which favor the use of PET: it is a simple technique compared with invasive histological sampling, there is a low patient dose as a single examination and with carefully chosen indications it provides accurate results.

The activities in the research of imaging agents are promising (Buscombe et al. 2006), and possibly the development of new and improved tracer agents will offer further possibilities to innovate and advance PET and hence change indications and use of this diagnostic tool.

5.6 Combined PET/CT Imaging

The evolution of fused PET/CT imaging, also known as hybrid imaging, is particularly promising, since it combines the advantages of a detailed imaging of the anatomy combined with detection of local metabolic activity pattern; hence, for the first time, this technique offers simultaneously direct information of form and function of bone pathology (Figs. 5.1, 5.2). The information acquired by this diagnostic procedure will inevitably help the treating physician to optimize initial therapy and follow-up treatment. Especially the planning of surgical therapy, if necessary, can be achieved more precisely in advance compared with the use of CT and conventional bone scans. Especially in cases of primary chronic osteomyelitis it is desirable to obtain a representative biopsy from an area with disease activity. The fusion images of the PET/CT scan can give the surgeon a most precise

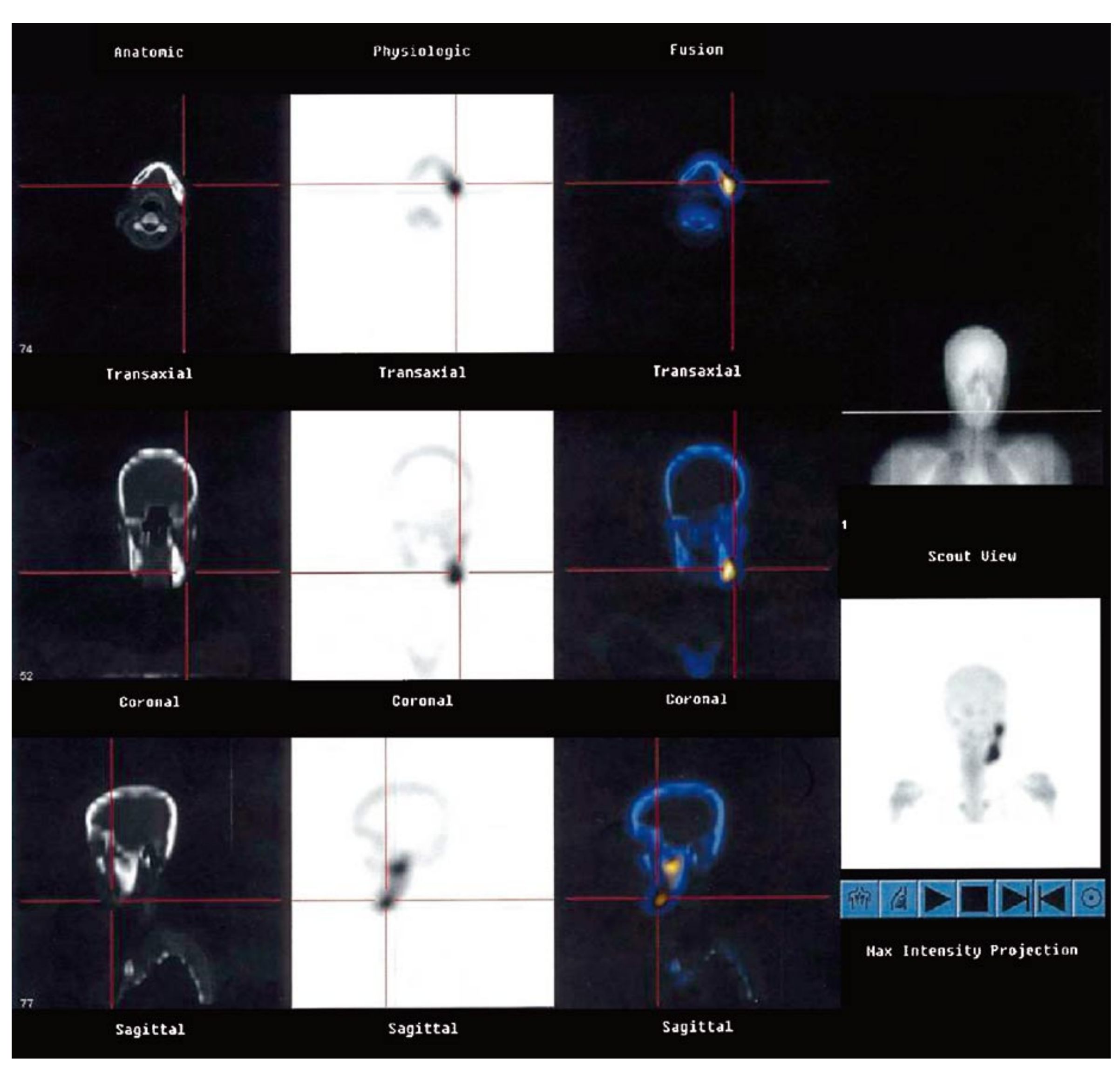


Fig. 5.1 Combined ^{18}FDG PET/CT scan of a patient with primary chronic osteomyelitis of the mandible. The hybrid scan allows the exact anatomical outlining of the affected region with an increased metabolic activity. The Corresponding Tc-99M bone scan does not demonstrate an exact anatomical distribution of the affected area. (This case is described in detail in Chap. 12, case report 16)

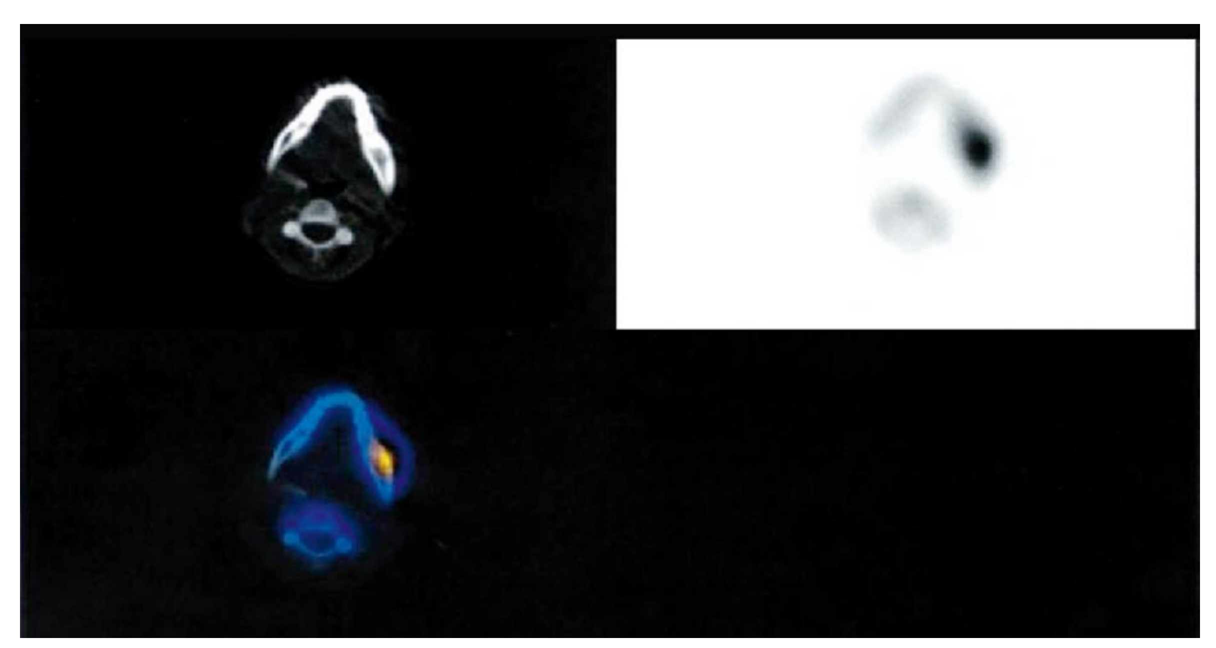


Fig. 5.2 Combined ^{18}FDG PET/CT scan of a patient with primary chronic osteomyelitis of the mandible. The hybrid scan allows the exact anatomical outlining of the affected region with an increased metabolic activity. The Corresponding Tc-99M bone scan does not demonstrate an exact anatomical distribution of the affected area. (This case is described in detail in Chap. 12, case report 16)

map of the desired location. Possible combination with navigation systems will even increase the accuracy in the near future.

With the increasing availability and use of these combined PET/CT scanners, multimodality imaging (Nuclear Medicine/Radiology) will progress into clinical routine diagnostics, broadening our experience in diagnosing various pathologies including osteomyelitis of the jaws. The advantages of this technique are becoming more apparent and perhaps we are looking at the future gold standard in the diagnosis of osteomyelitis of the jaws.

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Pathology of Osteomyelitis

Elisabeth Bruder, Gernot Jundt, Gerold Eyrich

Contents

6.1 Summary

According to the Zurich classification on osteomyelitis of the jaws, pathology is considered a secondary classification criterion. Pathology serves to confirm the diagnosis of osteomyelitis if clinical judgment and diagnostic imaging studies are not conclusive. Histology of jaw osteomyelitis should always be complemented and interpreted in conjunction with clinical and radiological findings and should not be used independently. Importantly, it is an essential tool to exclude differential diagnoses such as malignant tumors, fibrous dysplasia, and other tumor-like lesions. Harvesting biopsy specimens from a representative area, correct tissue submission and tissue preparation are prerequisites to obtain a conclusive histology.

Histopathology of acute and secondary chronic osteomyelitis encompasses the full scope of inflammatory infiltrates ranging from mainly inflammatory exudate composed of fibrin, polymorphonuclear leucocytes and macrophages in the acute stage, to a predominant plasma cell infiltration accompanied by a variable extent of marrow fibrosis. A clear distinction from primary chronic osteomyelitis to secondary chronic osteomyelitis solely based on histopathology is not always possible; however, in context with clinical presentation and imaging studies, histology contributes to specify the diagnosis of chronic osteomyelitis. Furthermore, "specific" osteomyelitis is defined by a histological picture with granulomatous inflammatory response to specific pathogens, such as *Mycobacteria*, and necessitates adequate therapy.

6.2 Introduction

Osteomyelitis of the jaws comprises a spectrum of disorders that are mainly defined on a clinical, radiological, pathological, and etiological bases as described in detail in the pertinent chapters of this book. The Zurich classification introduced is based primarily on clinical appearance and course of disease, as well as on radiological features. Pathomorphology is considered a secondary classification criterion (Table 6.1).

Three main groups of osteomyelitis of the jaws are distinguished:

1. Acute osteomyelitis
2. Secondary chronic osteomyelitis
3. Primary chronic osteomyelitis

Histopathology forms an important classification criterion and supports the distinction of the main three

Table 6.1 Classification criteria upon which the Zurich classification of osteomyelitis is based

Hierarchic order of classification criteria	Classification criteria	Classification groups
First	Clinical appearance and course of disease Radiology	Major groups Acute osteomyelitis (AO) Secondary chronic osteomyelitis (SCO) Primary chronic osteomyelitis (PCO)
Second	Pathology (gross pathology and histology)	Differentiation of cases that cannot clearly be distinguished solely on clinical appearance and course of disease; important for exclusion of differential diagnosis in borderline cases
Third	Etiology Pathogenesis	Subgroups of AO, SCO, and PCO

categories in the Zurich classification; however, histology needs to be complemented and interpreted in conjunction with clinical and radiological findings and should not be used independently on its own.

An important purpose of histopathological investigation – beyond the confirmation of a clinically and radiologically suspected diagnosis of osteomyelitis – consists of typing and grading of the inflammatory activity. This may be of help in distinguishing secondary chronic osteomyelitis from primary chronic osteomyelitis in some instances where the clinical course and imaging studies are not conclusive. Similarly, differentiation from other pathologies is accomplished by histology.

The imaging aspect of acute and both primary and secondary chronic osteomyelitis may further resemble an aggressive tumor; therefore, histopathology serves as an important tool to rule out the differential diagnosis of neoplasia.

This chapter deals with the main morphological aspects of osteomyelitis as found in the jaws. Morphological features are illustrated in detail. The pathological description of osteomyelitis in this chapter follows the Zurich classification. Essentials of differential diagnosis are also discussed.

6.3 Tissue Submission

Whenever a patient undergoes maxillofacial surgery, all tissue removed from a patient is best and most competently handled by an expert pathology department. Tissue submitted for pathological investigation either results from diagnostic biopsy, therapeutic curettage, or surgical resection. Either way, tissue is best submitted rapidly (within 30 min), fresh and native unfixed on water ice (0–4°C), so as to permit optimal microbiological as well as molecular investigation. Microbiological culture will facilitate antimicrobiological treatment of osteomyelitis. Molecular investigation is currently not indicated for the diagnosis of osteomyelitis by itself, but serves to exclude or confirm a differential diagnosis of a neoplasia, in particular Ewing tumors, lymphomas, and leukemias.

Tissue processing usually follows standard procedures: bone is fixed in formalin, carefully decalcified in a chelating agent, such as EDTA, and subsequently paraffin embedded. For a diagnosis of osteomyelitis, routine stains are applied: hematoxylin–eosin (H&E); van Gieson; Giemsa; and PAS. If necessary, immunohistochemistry can be performed on paraffin sections after antigen retrieval by enzymatic, temperature, or microwave methods; however, a routine diagnosis of osteomyelitis is made by conventional histology on an H&E slide alone. Subsequently, special stains are applied to look for potential microbial organisms.

Although tissue processing follows standard protocols for investigation of bone, some expert laboratories specialized in handling of bone will achieve better morphological results. It is therefore recommended to send bone biopsies, curettage, and resection specimens to specialized pathology centers, just as patients are being referred to centers of competence for expert maxillofacial treatment.

6.4 Macroscopic Pathology

In osteomyelitis, surgical therapy intends to remove necrotic bone by “debridement.” Macroscopy of specimens removed for osteomyelitis is determined by the type of surgery and depends on the extent and duration of disease (Figs. 6.1, 6.2).

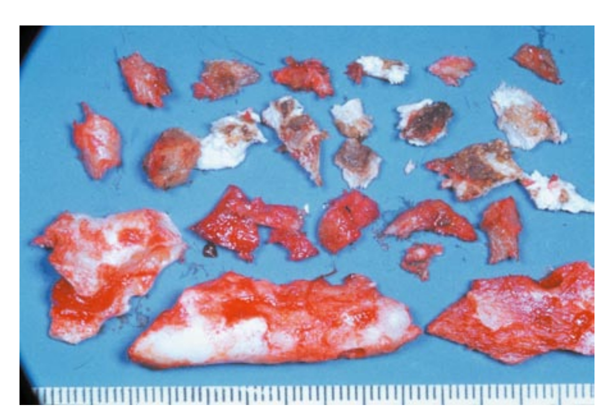


Fig. 6.1 Multiple sequesters surgically removed in a case of extensive secondary chronic osteomyelitis of the mandible (Courtesy of N. Hardt)

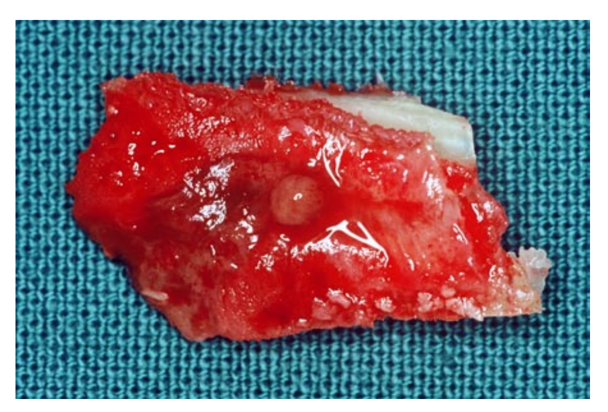


Fig. 6.2 Large bone sequester removed in a case of secondary chronic osteomyelitis with adjectant granulation tissue (Courtesy of N. Hardt)

Curettage yields small tan to brown hemorrhagic bone fragments and beige inflammatory exudate (Fig. 6.1). Small curettage fragments are usually totally embedded in paraffin and normally do not require dissection. Larger tissue specimens should be oriented and cut perpendicularly to the osseous surface. Necrotic bone fragments are pale whitish-gray. Sequesters usually show an irregular outline (Figs. 6.1, 6.2).

Occasionally, a jaw resection is required. On cross section, the bony cortex appears thickened, and the cancellous bone sclerosed. Osteolytic and osteosclerotic foci may alternate.

If a biopsy is performed in order to confirm a diagnosis of osteomyelitis and to rule out neoplasia, the amount of tissue submitted may be very small and only a minute biopsy is received. In such cases of an elective biopsy, it is important to be aware of minimal tissue requirements to reach a conclusive diagnosis. Ideally, patients are discussed in a prebiopsy interdisciplinary setting with the pathologist involved early in the diagnostic process and treatment plan.

6.5 Microscopic Pathology

6.5.1 Nonspecific Osteomyelitis

6.5.1.1 Acute (Suppurative) Osteomyelitis

Acute (suppurative) osteomyelitis is defined as a suppurative infectious disease of bone. It can be hematogenous (i.e., endogenous) or caused by local extension of a neighboring infection. In the jaws, it is most frequently caused by local extension of an odontogenic infection.

Morphologically, acute (suppurative) osteomyelitis is characterized by an inflammatory exudate composed of fibrin, polymorphonuclear leucocytes, and macrophages (Fig. 6.3a). The inflammation is located primarily in the medullary spaces of the spongiosa but secondarily involves the spongiosa trabeculae and can penetrate the cortex and reach the periosteum.

Marrow spaces are filled with neutrophils, necrotic debris, and microorganisms. Marrow fatty tissue and hematopoietic marrow have undergone necrosis and are replaced by inflammatory exudate (Figs. 6.3b–6.3d). Pressure in the medullary space is increased and blood vessels are destroyed. As a result, compromised vascular perfusion leads to necrosis of spongiosa and cortex. Necrotic lamellar bone trabeculae are hypereosinophilic and lamellation is blurred. Osteocytes undergo necrosis and osteocyte lacunae appear empty from 2 weeks onward. Osteocyte process channels and osteocyte lacunae are enlarged with dark-blue margins.

Sequester formation may ensue (Jundt 2004). The sequestrum will frequently be colonized with biofilm-forming microorganisms that then perpetuate the inflammation and lead to secondary chronic (suppurative) osteomyelitis beyond a 1-month duration. Periosteal elevation is followed by periosteal new bone formation. Complications include fistula formation and in rare instances suppurative arthritis.

The microorganism most frequently responsible for osteomyelitis of long bones is *Staphylococcus aureus* (85%). This is a Gram-positive cocciform bacte-

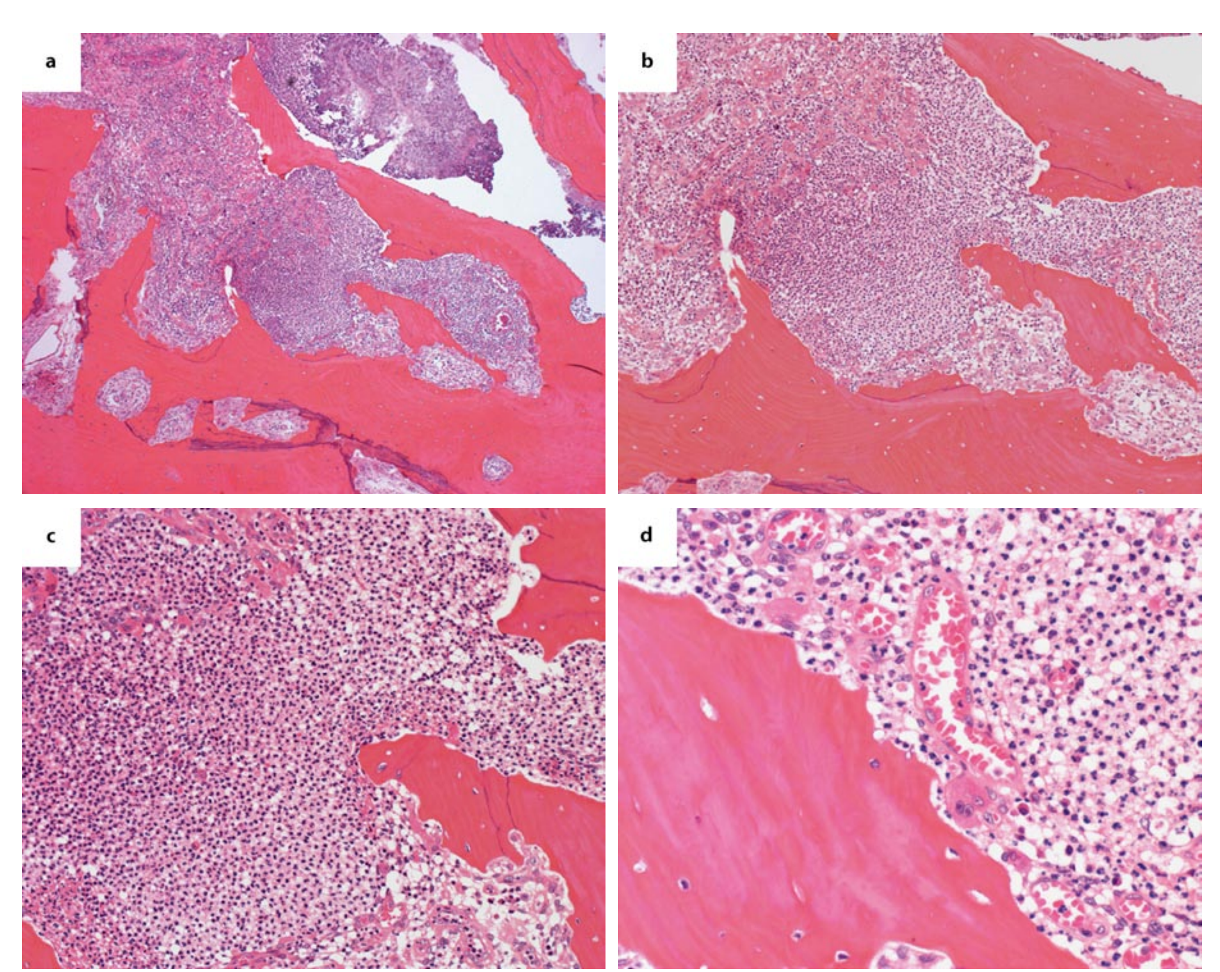


Fig. 6.3a–d Acute (suppurative) osteomyelitis (H&E stains). **a** Low-power magnification of jaw with acute destructive suppurative osteomyelitis. **b** Medium-power magnification shows absence of fatty marrow and dense inflammatory marrow infiltrate. **c** Marrow spaces are occupied by neutrophils. Bone trabeculae show an irregular contour due to osteoclast resorption. **d** High power of active osteoclasts and partial bone necrosis

rium. *Staphylococcus aureus* is usually demonstrable in the paraffin section by a Gram stain. In osteomyelitis of the jaws, *Staphylococcus*, *Streptococcus*, and *Actinomyces* species are causative agents in the majority of patients. *Staphylococcus* and *Streptococcus* species are visible on H&E or Gram stains. *Actinomyces* is demonstrated by PAS and Gram staining. Microorganisms preferably colonize necrotic bone and form large colonies that spread within lacunae and channels on bone surfaces.

6.5.1.2 Chronic Osteomyelitis

Chronic osteomyelitis has been subject to controversial attempts at classification. These attempts have not only followed clinical lines, but particularly in German-speaking countries, such classification attempts have been based on histology (Garrè 1893; Uehlinger 1977; Jani and Remagen 1983; Jundt 1997).

In this book, we follow the three-tiered Zurich classification of osteomyelitis of the jaws with distinction of acute osteomyelitis as well as secondary and primary chronic osteomyelitis. As presented previously in this chapter (Table 6.1), histology is considered a secondary criterion in this classification system. Morphology (macroscopic and microscopic) alone cannot clearly distinguish between secondary and primary forms of chronic osteomyelitis; however, in the context with clinical presentation and imaging studies, histology contributes to specify the diagnosis of chronic osteomyelitis.

6.5.1.3 Primary Chronic Osteomyelitis

The morphological picture of primary chronic osteomyelitis is governed by the involved components inflammatory infiltrate, mesenchymal marrow reaction (fibrosis), and secondary osseous alterations (osteolysis or sclerosis; Figs. 6.4a–6.4c).

The inflammatory infiltrate consists of plasma cells that may even be predominant. Neutrophilic granulocytes form a variable, mostly minor proportion (Jundt 1997; Eyrich et al. 2003). Lymphocytes and macrophages are also present. Edema of marrow spaces may be a prominent finding. Even if the type of inflammatory response has not been found to reliably predict the clinical course of the disease (Jundt 1997), it nevertheless may provide an important clue toward activity of disease.

Marrow fibrosis will ensue after fibroblast growth factor release and may either be loose and minor or dense and prominent. The range of secondary osseous alterations is enormous (Figs. 6.4c, 6.4d). Reactive new bone formation may be massive and lead to prominent reactive host bone sclerosis. Osteoblastic activity may be pronounced and lead to increased caliber of intralesional and surrounding medullary trabeculae. With osteoclast activation and repeated episodes of reactive bone formation, a characteristic irregular pattern of reversal lines ensues resembling that observed in Paget's disease (Figs. 6.4d–6.4f). This pattern is therefore described as "pagetoid." In such cases of prominent reactive bone formation, histology is characterized by massive sclerosis of cancellous bone, accompanied by periosteal new bone formation and cortical sclerosis. The involved skeletal elements may be expanded.

We have previously described the formation of neutrophilic microabscesses in the diffuse sclerosing chronic osteomyelitis subtype of primary chronic osteomyelitis (Eyrich et al. 2003). These microabscesses are interpreted as sign of active stage of disease and correlated well with a mixed osteolytic and osteosclerotic picture on radiology (Eyrich et al. 2003).

Microabscess formation is observed in patients of all ages with pure mandibular manifestation of primary chronic osteomyelitis, although in our series of patients we observed a higher incidence in children and young adults (e.g., early-onset primary chronic osteomyelitis). Microabscess formation is, however, most prominent in patients with additional dermoskeletal involvement (e.g., syndrome-associated primary chronic osteomyelitis; Baltensperger et al. 2004). A higher rate of bone resorption and subperiosteal bone formation is noted more often in younger individuals and in an early stage of disease. In contrast, medullary fibrosis and endosteal bone apposition with pagetoid appearance are more prominent in elderly patients and in advanced disease stages (Baltensperger et al. 2004).

A recent publication by Montonen et al. (2006) examined the immunohistopathology of patients with primary chronic osteomyelitis compared with bone from healthy individuals. The authors described the role of receptor activator of nuclear factor KB ligand (RANKL)-driven osteoclastogenesis and the acidic cysteine endoproteinase cathepsin K in the pathogenesis of primary chronic osteomyelitis. Both proteins act as promoters of osteoclast-mediated bone resorption which may represent the primary disease process, which is later followed by new bone formation.

It is important to recognize that the histological picture of chronic osteomyelitis is currently not regarded as specific for any subtype; therefore, the diagnosis and subtyping requires the interpretation in conjunction with clinical, radiological, microbiological, and pathological findings. For this, the syndrome of synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) is a prominent example showing histology of chronic sclerosing osteomyelitis (Chamot 1986; Eyrich 2000).

6.5.1.4 Secondary Chronic Osteomyelitis

By definition, acute osteomyelitis becomes "secondary chronic" after duration of 1 month (Mercuri 1991; Marx 1991). Acute osteomyelitis and secondary chronic osteomyelitis are therefore considered to be the same disease at different stages. Both acute and secondary chronic osteomyelitis are considered true bone infections that are accompanied with more or less extensive suppuration. Complications of secondary chronic osteomyelitis predominantly include formation as well as development of bone sequester. Histopathology in cases of secondary chronic osteomyelitis with significant suppuration will demonstrate similar features as cases of acute osteomyelitis with large amounts of polymorphonuclear leucocytes, macrophages, and plasma cells, accompanied by a variable degree of marrow fibrosis and reactive bone formation. In cases of secondary chronic osteomyelitis with a less fulminate (e.g., more chronic) course, marrow fibrosis and reactive bone scleroses are predominant (Fig. 6.5a–f). In some instances, provided there is proper staining and magnification, bacteria may be identified on histopathological specimens. In cases of secondary chronic osteomyelitis of the jaws caused by

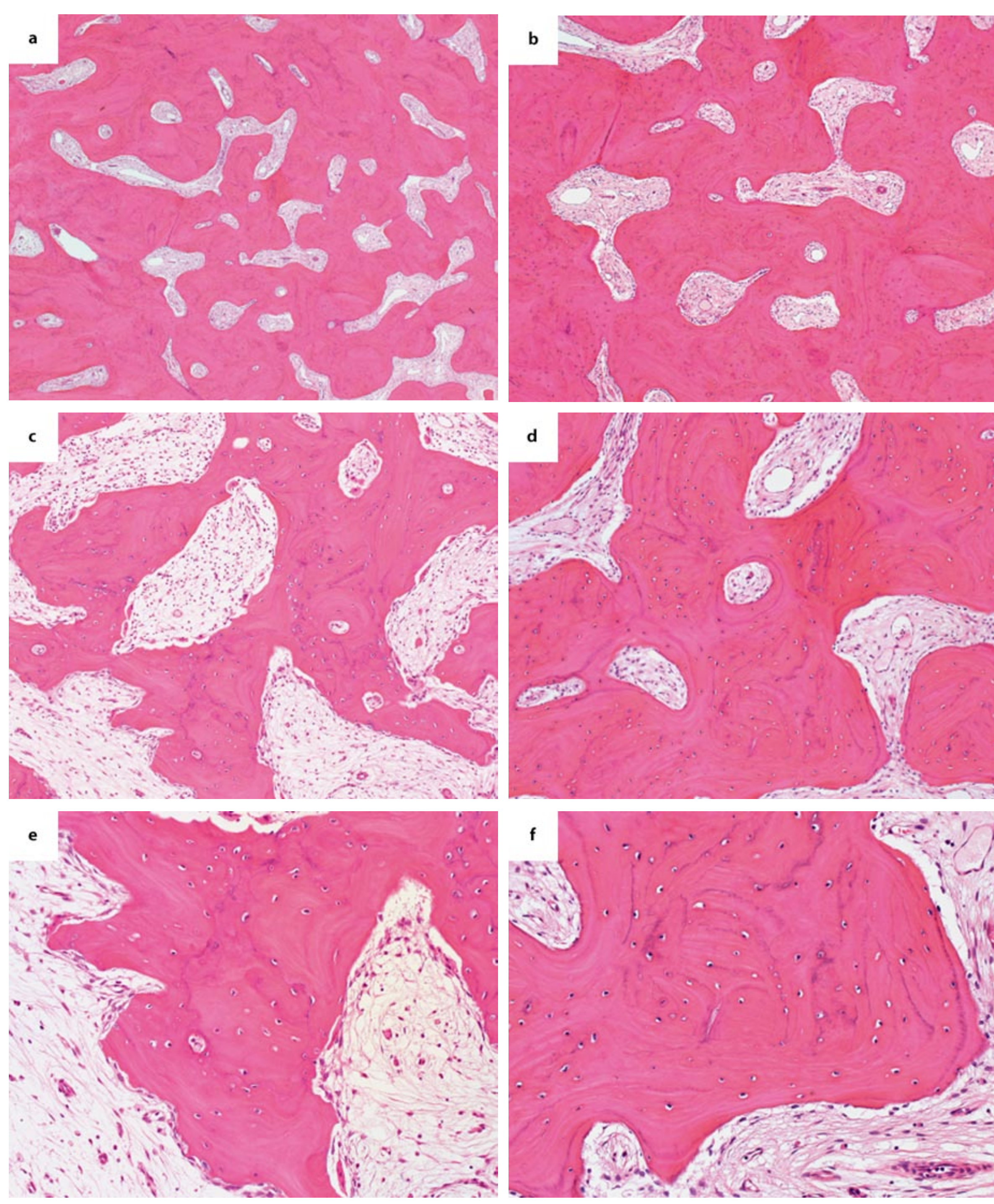
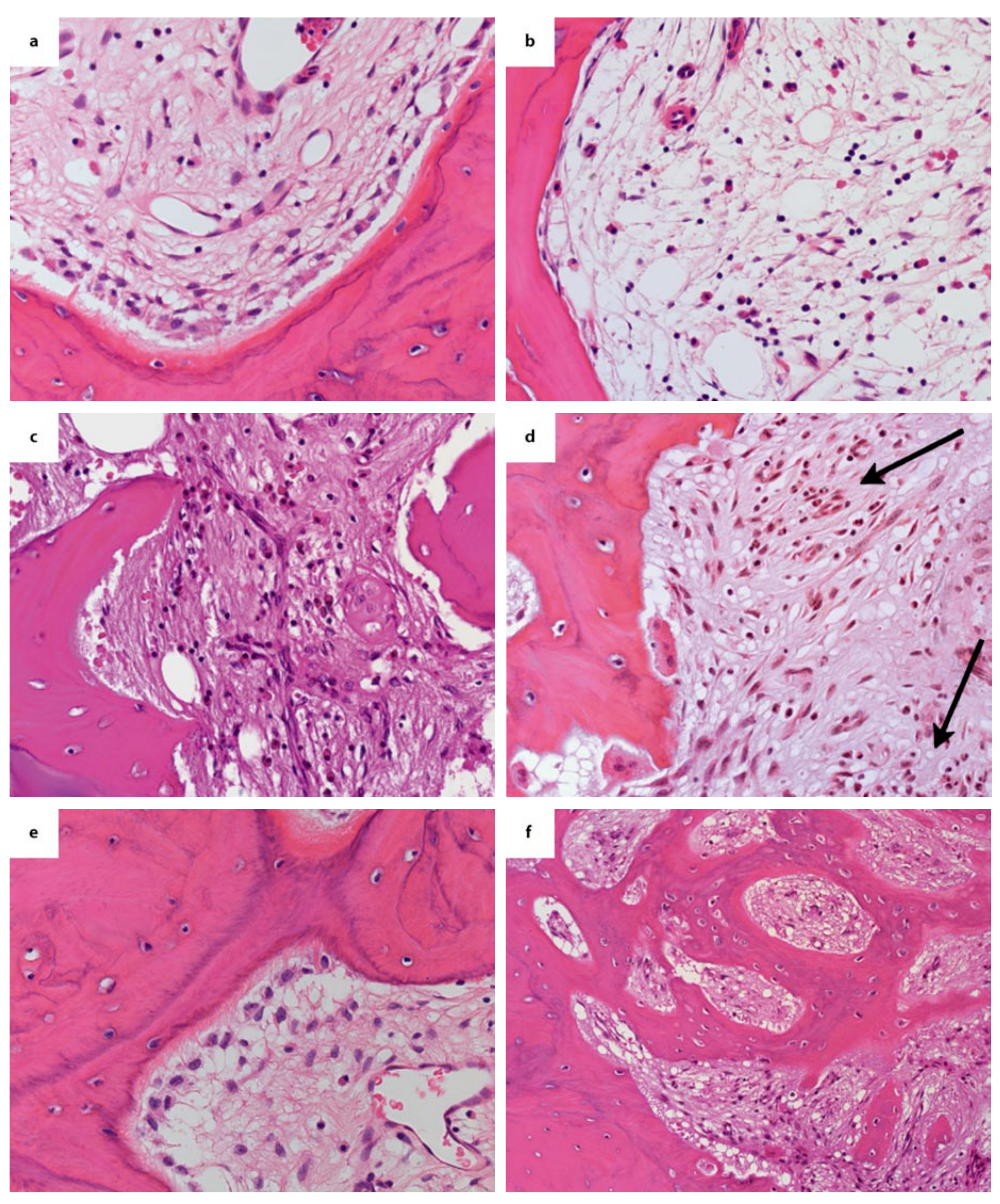


Fig. 6.4a–f Primary chronic osteomyelitis (H&E stains; specimens collected from different patients). **a** Low-power magnification of bone sclerosis. **b** Medium-power magnification reveals absence of fatty tissue in narrowed marrow spaces. **c** Active osteoclast resorption of bone trabeculae results in irregular trabecular contour with multiple adjacent Howship lacunae. **d** Repeated episodes of bone resorption and reactive bone formation lead to an irregular "pagetoid" reversal line pattern similar to that in Paget's disease, and marrow spaces show loose fibrosis. **e,f** Irregular "pagetoid" reversal lines, loose marrow fibrosis



■ **Fig. 6.5a–f** Patient with secondary chronic osteomyelitis (H&E stains). **a** High-power magnification of marrow space and adjacent bone trabeculae shows absence of fatty tissue with loose marrow fibrosis and scattered lymphocytic inflammatory infiltrates. Bone trabeculae are lined by reactive osteoblasts and newly formed osteoid seams. **b** High-power magnification of another marrow space reveals loose fibrosis of marrow with scattered lymphoplasmocytic inflammatory infiltrates. **c** Plasmocytic predominant inflammatory infiltrate. **d** Loose marrow fibrosis with some scattered inflammatory cells and neutrophil aggregates ("microabscesses"; *arrows*). **e** High-power magnification of active osteoblast seam, loose marrow fibrosis, and scattered occasional lymphocytic inflammatory cells. **f** Reactive periosteal woven bone formation

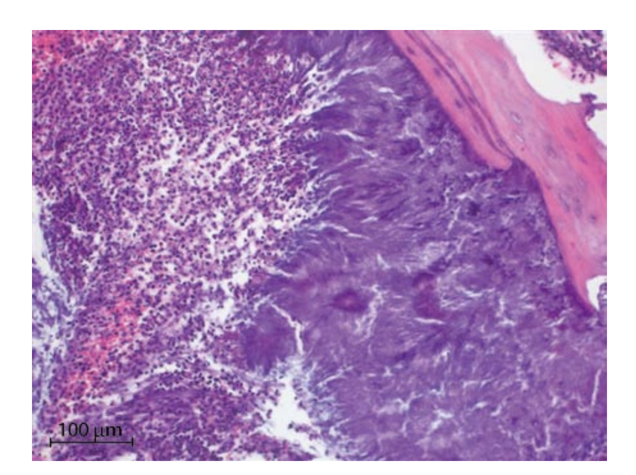


Fig. 6.6 Tissue specimen collected from the surgical site shows abscess formation and actinomyces "drusen" (H&E stain; courtesy of R. Flury). (This patient is described in detail in Chap. 12, case report 11)

Actinomyces, "drusen" formation can be observed, classical for this type of infection (Fig. 6.6).

As mentioned in Chap. 2, some patients with secondary chronic osteomyelitis present with little pus, fistula, and sequester formation, or may even lack these symptoms at a later stage of disease. The fewer clinical signs of suppuration are evident, the more histopathology will resemble the typical appearance of chronic osteomyelitis with no clear distinction of primary and secondary chronic forms.

The most important complication of secondary chronic osteomyelitis of long bones is systemic amyloidosis; however, this is rarely observed in cases involving the jaws. Furthermore, over the past decades, systemic amyloidosis as a consequence of chronic osteomyelitis has been steadily decreasing with the advent of powerful antibiotic treatment.

6.5.2 "Specific" Osteomyelitis

The "specific" osteomyelitis forms are rare. In the Zurich classification as advocated in this book, they are incorporated as cases of acute or secondary chronic osteomyelitis, as described in extent in Chap. 2. They are result of infections with mycobacteria, spirochaetae, or of a manifestation of sarcoidosis. Mycobacterial infection is most common and most often affects the vertebral column (Jundt 2004); however, jaw involvement, particularly of the mandible, has repeatedly been described (Chaudhary et al. 2004; Lachenauer et al. 1991; Taylor and Booth 1964). It leads to a specific inflammatory response with granuloma formation. Epithelioid-giant cell granulomas with caseating necrosis are the core elements of pathology in mycobacterial infection. The diagnosis of mycobacterial infection is confirmed by demonstration of acid-fast bacilli in the Ziehl Neelsen stain on paraffin section. However, microorganisms may be scarce and may not be demonstrable by conventional histology; therefore, more sensitive special techniques have been developed. The presence of mycobacterial DNA may be proved by polymerase chain reaction performed on DNA extracted from paraffin-embedded tissue (Höfler 1994; Huggett et al. 2003; Ikonomopoulos et al. 1999). Polymerase chain reaction is a rapid and comparatively inexpensive technique combined with high sensitivity. Nevertheless, as a result of formalin fixation and decalcification, particularly on acid basis, the quality of DNA extracted from such tissue may not be optimal and the PCR therefore false negative. In such cases, microbial culture from fresh tissue remains the gold standard of identification of the responsible mycobacterial microorganism.

6.6 Differential Diagnosis

6.6.1 Tumors

6.6.1.1 Ewing Tumor Group

Ewing tumors, such as Ewing sarcoma (Fig. 6.7a–c), are characterized by a prominent reactive lamellar periosteal new bone formation, which may also occur in primary and secondary chronic osteomyelitis. Crushing artifact and tumor necrosis may obscure scattered Ewing tumor cell infiltrates and render a differential diagnosis extremely difficult, especially in the absence of immunohistochemistry; therefore, adjunctive diagnostic techniques, such as immunohistochemistry or even molecular search for a specific Ewing tumor translocation, may be mandatory in a biopsy in an appropriate setting.

6.6.1.2 Langerhans Cell Histiocytosis

Langerhans cell histiocytosis may be associated with a prominent inflammatory infiltrate, particularly eosinophilic granulocytes. Demonstration of aggregates of Langerhans cells as visualized by immunohistochemistry for CD1a and S100 are regarded as diagnostic for Langerhans cell histiocytosis.

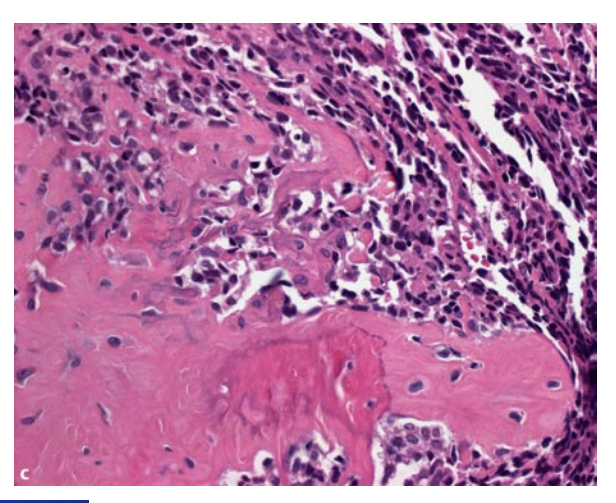




Fig. 6.7a–c Ewing sarcoma of the mandible. **a,b** Macroscopic aspect of a partially resected mandible affected with Ewing sarcoma. **c** Ewing sarcoma histology (H&E stain)

6.6.1.3 Osteosarcoma

Osteosarcoma may enter the differential diagnosis if the inflammatory infiltrate is scarce and bone consists of predominantly woven trabeculae. In osteosarcoma, the neoplastic tumor stroma shows moderate to marked nuclear atypia and atypical mitotic figures.

6.6.2 Vascular Lesions

Vascular lesions may predispose to osteomyelitis and may be obscured by the resulting inflammatory infiltrate and tissue alterations. Immunohistochemical investigations may be necessary to reach a conclusive diagnosis and correct subtype of an underlying vascular lesion.

6.6.3 Vascular Malformations

Lymphatic malformations, particularly generalized lymphatic malformations, may be associated with inflammation and even predispose to osteomyelitis. Immunohistochemical expression of D2-40 is considered as specific for lymphothelium lining lymphatic vascular channels.

6.6.4 Vascular Tumors

In epithelioid hemangioma, the intervascular tumor stroma typically contains inflammatory cells, predominantly eosinophilic granulocytes. Immunohistochemistry may be indicated to highlight the neoplastic vessels with their characteristic eosinophilic, epithelioid, and hobnailed endothelia.

6.6.5 Osteopetrosis

Osteomyelitis of the jaws may be the presenting symptom of osteopetrosis, particularly the autosomal-dominant form (Junquera et al. 2005). It is important to be aware of the possibility of this underlying condition. In osteopetrosis, osteoclast formation and osteoclast function are impaired resulting in insufficient or absent bone resorption (Balemans et al. 2005); therefore, morphologically, osteopetrosis is characterized by absence of medullary spaces and bone remodeling with increased thickness of medullary bone trabeculae and of the bone cortex (Bruder et al. 2003). In autosomal-recessive osteopetrosis, primary spongiosa persists with cartilaginous cores surrounded by primary osteoid and lamellar bone.

Osteopetrosis leads to impingement on cranial nerves, and thickening of calvarial bone and maxillofacial skeletal elements, including the alveolar lamina dura. Tooth eruption is defective, and some teeth may be absent or malformed with enamel hypoplasia and disturbed dentinogenesis.

6.6.6 Fibro-osseous and Tumor-like Lesions

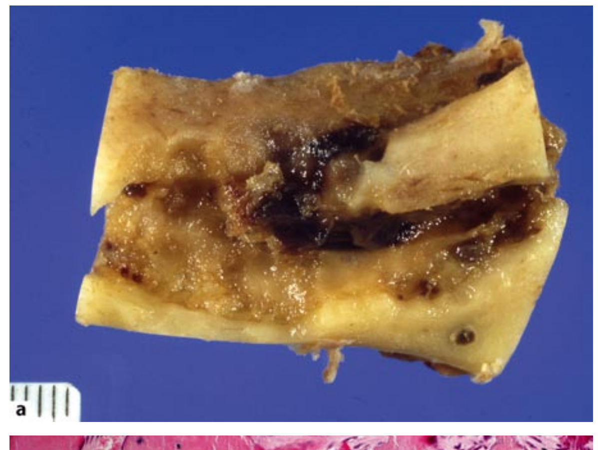
Occasionally, nonossifying fibroma, ossifying fibroma (Fig. 6.8a–c), and solitary bone cyst may also enter the differential diagnosis. These lesions are usually easily distinguished from osteomyelitis and are not biopsied, if the radiological aspect is typical, and are therefore also called "leave me alone lesions." However, in an atypical setting, they may require biopsy for diagnostic security. It is as such in their atypical presentation that they may occasionally need to be distinguished from chronic osteomyelitis.

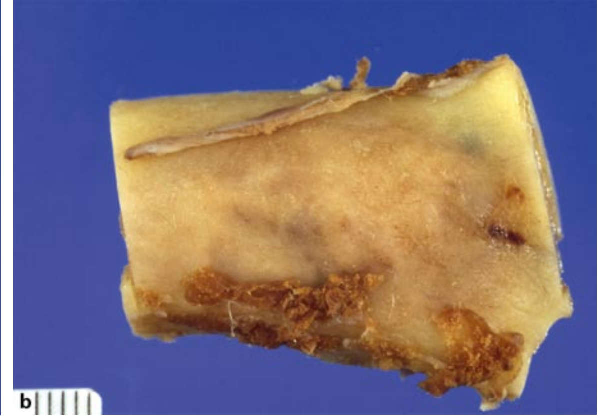
6.6.7 Fibrous Dysplasia

Fibrous dysplasia of the jaw is considered to be a disease entity of its own. In certain cases the affected bone may be superinfected and show additional signs of osteomyelitis. Fibrous dysplasia is caused by somatic activating guanine nucleotide-binding protein alpha-stimulating activity polypeptide 1 (*GNAS1*) mutations (Idowu et al. 2007). Fibrous dysplasia is a benign medullary fibro-osseous lesion with solitary, monostotic or multifocal, polyostotic involvement. Fifty percent of patients with fibrous dysplasia are diagnosed in the first two decades of life. A female predominance is often reported. Ten to 15% are polyostotic and manifest in the first decade. There is no geographic or racial predilection.

Polyostotic fibrous dysplasia is intimately associated with the McCune-Albright syndrome with endocrine abnormalities and skin pigmentation. A relationship of fibrous dysplasia with intramuscular myxomas exists in Mazabraud syndrome.

Sites of involvement are predominantly the long bones in female patients, and ribs and skull in male patients. In monostotic fibrous dysplasia, 35% are located in the skull (Fig. 6.9a), another third in the femur and tibia, and 20% in the ribs. In polyostitic fibrous dyspla-





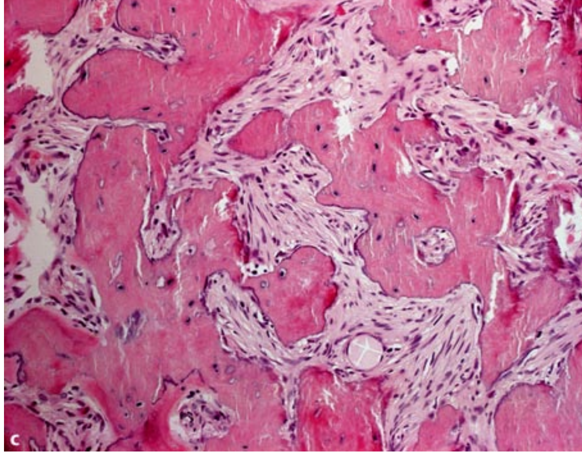


Fig. 6.8a–c Ossifying fibroma of the mandible. **a,b** Macroscopic aspect of a partially resected mandible affected with an ossifying fibroma. **c** Ossifying fibroma histology (H&E stain)

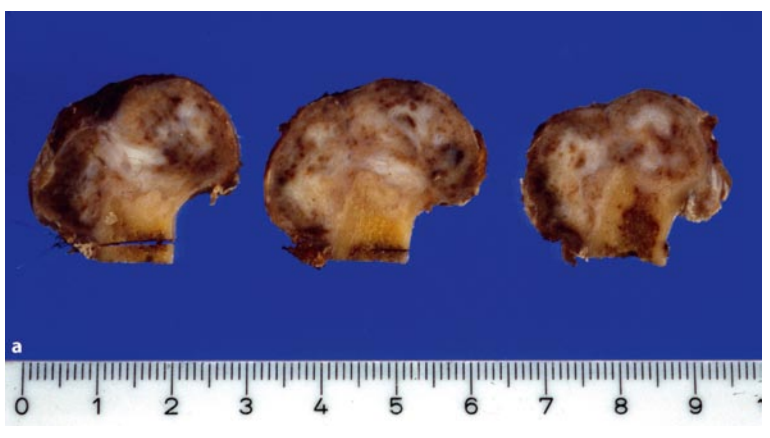
sia, involvement most frequently affects the femur, the pelvis, and the tibia in the majority of cases. Fibrous dysplasia is often asymptomatic but may be painful or fracture.

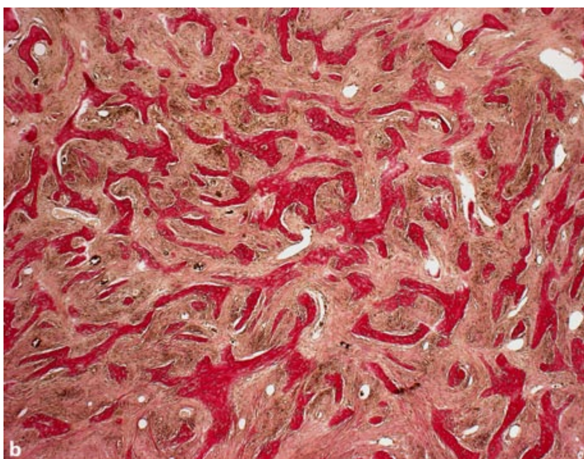
Radiographically, fibrous dysplasia is characterized by a nonaggressive geographic osteolysis with ground glass matrix. There may be expansion, but there is usually no soft tissue extension and no periosteal reaction unless fractured.

Histologically, fibrous dysplasia is characterized by immature woven bone trabeculae without osteoblastic rimming, scattered in a fibroblastic stroma yielding a "Chinese soup" pattern (Fig. 6.9b, 6.9c). The osseous component may form cementum-like psammomatous particles in some cases. The stroma is variably cellular and composed of triangular fibroblastic elements and thin-walled variably prominent blood vessels. There may be a cartilage component in fibrocartilaginous dysplasia and secondary aneurysmal bone cyst formation or foam cell change may occur.

Similar to osteochondroma, solitary as well as multifocal forms have been described and have been linked to somatic activating mutations of the guanine nucleotide-binding protein alpha-stimulating activity polypeptide 1*GNAS1* gene. The missense mutation affects codon 201 and leads to a substitution of Arginin with Histidin in the μ-subunit of the signal-transducing stimulatory G-protein. Recently, a mutation of codon 227 has also been described (Idowu et al. 2007). Reported clonal chromosomal abnormalities have raised the suggestion of a neoplastic nature of fibrous dysplasia.

The differential diagnosis is low-grade central osteosarcoma: if the stroma is pleomorphic, the tumor shows mitotic activity and an aggressive growth pattern. Careful search for atypical nuclei and mitotic activity is essential for the diagnosis of well-differentiated osteosarcoma. Fibrous dysplasia can usually be recognized by its distinctly nonaggressive appearance on radiographs. Molecular confirmation of diagnosis is simple and rendered by polymerase chain reaction (Candeliere et al. 1997).





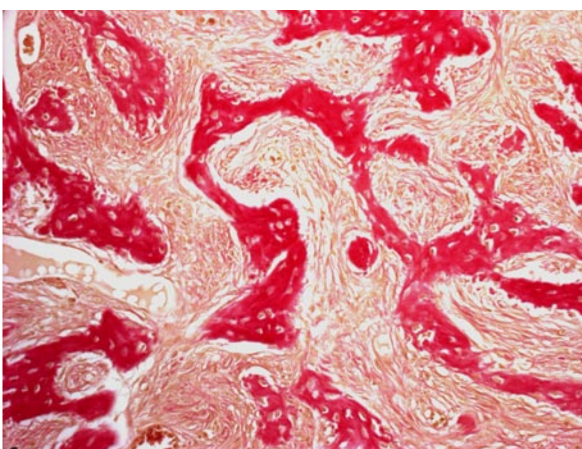


Fig. 6.9a–c Fibrous dysplasia of the mandible. **a** Macroscopic aspect of a partially resected mandible affected with fibrous dysplasia. **b** Fibrous dysplasia microscopic view with Chinese soup pattern (Van Gieson stain; low-power magnification). **c** Fibrous dysplasia with Chinese soup pattern (Van Gieson stain; high-power magnification)

6.6.8 Periapical Cemento-osseous Dysplasia

Periapical cemento-osseous dysplasia predominantly affects female patients and is almost always localized in the frontal region. Mostly, multiple teeth are involved: Initially, the lesion is poorly mineralized and presents as well-circumscribed, apical root-associated osteolysis. Progressive mineralization ensues, without enlargement. The associated tooth remains vital. Usually, periapical cemento-osseous dysplasia is self-limited and does not require further therapy.

6.6.9 Osteonecrosis

Osteonecrosis of the jaw is a complication of high-dose bisphosphonate application and is then referred to as osteochemonecrosis (Reid and Bolland 2007). It is characterized by exposed necrotic bone in the oral cavity. Suppression of bone turnover has been regarded as the relevant pathogenetic mechanism; however, loss of covering soft tissue has recently been attributed to soft tissue toxicity of the drug (Reid and Bolland 2007). The precipitating event is often an invasive procedure such as tooth extraction. Female patients older than 60 years are predominantly affected. Histologically, features consist of bone necrosis usually with no or only scarce signs of inflammation (Fig. 6.10). If necrotic bone becomes exposed to the oral cavity, bacterial colonization will take place, and if deep bone infection occurs, signs of secondary chronic osteomyelitis are noted.

Radionecrosis (radioosteonecrosis/osteoradionecrosis) shows histological features similar to those of osteochemonecrosis. Radionecrosis predominantly occurs in patients with high body-mass index, use of steroids, and radiation dose greater than 66 Gray (Goldwasser et al. 2007).

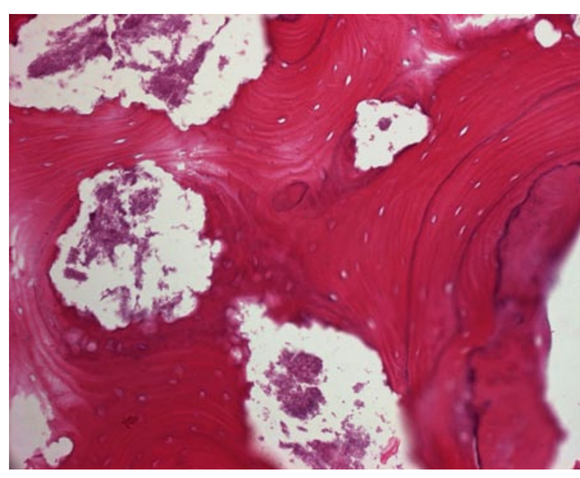


Fig. 6.10 Osteochemonecrosis in a female patient with bisphosphonate therapy (H&E stain at high-power magnification)

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Microbiology 7

Reinhard Zbinden

Contents

7.1 Summary

Microbiological investigations of specimens from anatomical structures adjacent to the oral cavity are always difficult to interpret concerning the relevance of the bacteria isolated. In case of an osteomyelitis of the jaws the detection of *Staphylococcus aureus* is often relevant and coagulase-negative staphylococci can be responsible for implant associated infections. Staphylococci are normally not found in the oral cavity; the susceptibility pattern of staphylococci is essential for adequate treatment; however, tissue samples as well as swabs from the infected jaw reveal mostly aerobic and anaerobic bacteria, e.g., viridans streptococci, *Eikenella corrodens*, peptostreptococci, *Fusobacterium* spp., and *Actinomyces* spp. All these bacteria can be innocent bystanders or infectious agents, but are mostly susceptible to clindamycin or amoxicillin–clavulanate; therefore, microbiological investigations are only helpful in case of osteomyelitis of the jaws, if specimens can be taken without contamination from the oral cavity. Furthermore, the laboratory must be informed if specific infections are suspected, e.g., actinomycosis, because selective agar plates must be inoculated and a prolonged incubation time up to 10 days is necessary. In case of a diagnosed primary chronic osteomyelitis of the jaws, interpretation of any isolated bacterium must be done with caution. Nevertheless, if the samples were taken without contamination from the oral cavity, the possible relevance of an unexpected bacterium should not be ignored.

In conclusion, routine microbiological investigations of osteomyelitis affecting the jawbone usually do not have a major clinical impact, unless a special clinical situation is present. In such cases, preanalytic precautions, i.e., sampling technique and transport media for anaerobes, must be respected; otherwise, microbiological results are not promising.

7.2 General Aspects of Microbiological Investigations of Specimens Normally Colonized by Bacteria

The main task of the microbiological laboratory is to detect infectious agents in the specimens sent to the laboratory. In case of samples from body compartments that are normally sterile, e.g., blood and CSF, optimal culture media and incubation conditions must be cho-

sen to find all infectious bacteria; however, even in these situations contaminating bacteria can be found. If a patient with pneumonia has in one of four blood culture bottles coagulase-negative staphylococci, they have to be considered as contaminants; however, a patient with an artificial heart valve with coagulase-negative staphylococci in four blood culture bottles (taken from two different sites) probably has an endocarditis.

In contrast to that, specimens from anatomical sites normally colonized with bacteria or specimens that come in contact with them will reveal a lot of bacteria that are not responsible for an infection. The microbiological technicians are well instructed to differentiate bacteria as normal colonizers or as potential infectious agents. For example, viridans (α-hemolytic) streptococci from the sputum are reported as normal flora of the oral cavity. A microbiological laboratory will not perform anaerobic cultures from the oral cavity because even more anaerobic bacteria than aerobic bacteria are normally present, especially in the gingival crevice (sulci) of the teeth.

In case of osteomyelitis of the jaws, the microbiological laboratories receive material that was in contact with the oral cavity and adjacent structures. Furthermore, during sampling the specimens can come in contact with normally present bacteria of the oral cavity. The microbiological laboratory will mostly find bacteria that are part of the normal flora; therefore, the microbiological findings can only have a clinical relevance if the bacteria found are not normal commensals. The oral microbiologists investigate the bacteria that are responsible of caries and periodontitis but those bacteria can also be found in case of osteomyelitis of the jaws without any specific pathological importance; therefore, the dentist is usually the first health care practitioner to see problems related to the mouth and masticatory apparatus, and to refer the patient to a specialist (Bernier et al. 1995).

7.3 Systematic and Susceptibility of Bacteria Found in Cases of Osteomyelitis of the Jaws

More than 200 microbial species have been cultured from the oral cavity of humans and between 400 and 500 additional taxa have been detected by 16S rRNA gene analysis of oral samples. Of these possible colonizers of the oral cavity (a total of more than 700), a limited number are present in the oral cavity of a healthy individual at any one time (Wilson 2005). Anaerobes normally reside in abundance as part of the normal flora with concentrations ranging from 10^9/ml in saliva to 10^{12}/ml in gingival scrapings. At this site, the ratio of anaerobic to aerobic bacteria ranges from 1:1 on teeth to 1000:1 in the gingival cervice (Tzianabos and Kaspar 2005). With the exception of *Actinobacillus actinomycetemcomitans* – which is well known as the responsible agent of juvenile periodontitis – mixed aerobic and anaerobic bacterial populations are present in periodontitis and can have access to the tooth supporting bone. Since Robert Koch, the aim of the applied methods in the traditional microbiological laboratory was to cultivate pure cultures. The Koch's postulates were based on pure cultures of a given bacterium that is associated with a special clinical entity and is not a commensal. Furthermore, the bacterium must induce the infection in an adequate transfer experiment to another host and the bacterium must be isolated again from the pathologically altered organ. Oral microbiologists have tried to investigate the pathogenesis of mixed aerobic and anaerobic bacteria in dental plaques for many years. These bacteria can theoretically have access to the underlying osseous structure of the jaws. Traditional clinical microbiology does not investigate mixed aerobic and anaerobic bacteria yet and can only isolate and describe the bacteria without any information as to which bacteria are clinically relevant.

The easiest way to categorize the most important and most frequent bacteria found in samples of osteomyelitis of the jaws is the coloration in the Gram stain and the preferred atmosphere (Table 7.1). *Staphylococcus aureus* and coagulase-negative staphylococci are not normally found in the oral cavity; the susceptibility pattern of staphylococci depends of the epidemiological situation and a susceptibility testing is mandatory. In contrast to that, all β-hemolytic and viridans streptococci are susceptible ampicillin or amoxicillin. The viridans streptococci can be divided in the mitis group, mutans group, salivarius group, and anginosus group (Ruoff et al. 2003). The anginosus group is also named *Streptococcus milleri* group with *Streptococcus anginosus*, *Streptococcus constellatus* subsp. *constellatus* and subsp. *pharyngis* and *Streptococcus intermedius*; this group is found in abscesses but often with mixed anaerobic flora. The presence of viridans streptococci in blood cultures may be associated with subacute bacterial endocarditis, especially in patients with prosthetic heart valves, with *Streptococcus sanguis*, *Streptococcus mitis*, *Streptococcus oralis*, and *Streptococcus gordonii* – all members of the mitis group – being frequently isolated. Members of the mutans group are associated with dental caries.

Table 7.1 Most frequently found bacteria in samples taken from patients with osteomyelitis of the jaws. Bacteria are categorized by coloration in Gram stain and the preferred atmosphere

	Facultative anaerobic	Anaerobic
Gram-positive cocci	*Staphylococcus aureus* Coagulase-negative staphylococci *Streptococcus* spp. *Abiotrophia* spp. *Granulicatella* spp.	*Peptostreptococcus* spp.
Gram-positive rods	*Actinomyces* spp. *Corynebacterium* spp. *Lactobacillus* spp. *Propionibacterium* spp. *Rothia dentocariosa*	*Actinomyces israelii* *Eubacterium lentum* *Bifidobacterium* spp.
Gram-negative cocci	*Neisseria* spp.	*Veillonella* spp.
Gram-negative rods	*Actinobacillus actinomycetemcomitans* *Capnocytophaga* spp. *Haemophilus* spp. *Eikenella corrodens* *Leptotrichia buccalis*	*Fusobacterium* spp. *Porphyromonas* spp. *Prevotella* spp.

Streptococcus salivarius can cause infections in neutropenic patients. The nutritionally variant streptococci were renamed as *Abiotrophia defectiva* and *Granulicatella adjacens* and are normally found in the oral cavity (Ruoff et al. 2003). The most important anaerobic Gram-positive cocci are the *Peptostreptococcus* spp., but a lot of them are reclassified in other genera; all of them are susceptible to amoxicillin–clavulanate but some are resistant to clindamycin (Moncla and Hillier 2003).

The facultative anaerobic Gram-positive rods found in the oral cavity and therefore in samples from the osteomyelitis of the jaws are listed in Table 7.1. Especially *Actinomyces* spp. and *Propionibacterium* spp. are often classified as anaerobic bacteria, but this is misleading because most of them can grow under aerobic conditions and are even resistant against metronidazole which is the standard antimicrobial agent against anaerobes. Amoxicillin–clavulanate is effective against all listed Gram-positive rods. Some isolates are resistant against clindamycin. Actinomycosis is a chronic infection characterized by abscess formation and tissue fibrosis and is mainly caused by *Actinomyces israelii* which is strictly anaerobic. *Actinomyces odontolyticus*, *Actinomyces naeslundii*, and the strictly anaerobic *Actinomyces meyeri* can also be responsible for an actinomycosis.

The Gram-negative cocci *Neisseria* spp. and *Veillonella* spp. are normal inhabitants of the oral cavity and are susceptible to amoxicillin clavulanate.

Fastidious facultative anaerobic Gram-negative rods of the so-called HACEK group, i.e., *Haemophilus* spp., *A. actinomycetemcomitans*, *Cardiobacterium hominis*, *E. corrodens*, and *Kingella kingae*, are normal inhabitants of the oral cavity and can be responsible for endocarditis. They are susceptible to combinations of amoxicillin and a beta-lactamase inhibitor, e.g., amoxicllin–clavulanate (Kugler et al. 1999); except *C. hominis*, all can be found in samples from osteomyelitis of the jaw. *A. actinomycetemcomitans* is now reclassified as *Haemophilus* and produces a number of toxins including (1) a leukotoxin that induces apoptosis in PMNs and macrophages, (2) a cytolethal distending toxin that inhibits host-cell cycle progression, (3) an immunosuppressive protein that inhibits lymphokine production by host cells, (4) an inhibitor of neutrophil chemotaxis, (5) a number of bone-resorbing factors, and (6) a collagenase (Wilson 2005). Since these pathogenic factors are involved in the juvenile periodontitis, a pathological role in osteomyelitis of the jaws can be assumed. *Leptotrichia buccalis* is also a normal facultatively anaerobic inhabitant of the oral flora and can be found in blood cultures of immunosuppressed patients.

The most important bacteria responsible for osteomyelitis of the jaws are the anaerobic Gram-negative rods, i.e., *Prevotella* spp., *Porphyromonas* spp., and *Fusobacterium* spp. Those are normal inhabitants of the oral cavity and most of them can produce a beta-lactamase

and are therefore resistant to penicillin but susceptible to the combination of amoxicillin–clavulanate or ampicillin–sulbactam; clindamycin is also mostly effective against Gram-negative anaerobic rods. All earlier pigmented *Bacteroides* spp. from the oral cavity were reclassified as *Porphyromonas* spp. and *Prevotella* spp. *Porphyromonas* spp. produce prophyrin pigments and are asaccharolytic, e.g., *Porphyromonas gingivalis*, *Porphyromonas endodontalis*, and *Prophyromonas asaccharolytica*. Saccharolytic *Prevotella* spp. can be pigmented, e.g., *Prevotella intermedia*, *Prevotella nigrescens*, *Prevotella melaninogenica*, *Prevotella loeschii*, *Prevotella corporis*, and *Prevotella denticola*, or nonpigmented, e.g., *Prevotella buccae*, *Prevotella buccalis*, *Prevotella oralis*, and *Prevotella oulorum*. Together with *Fusobacterium* spp. and other anaerobic Gram-negative rods, they are involved in the etiology of gingivitis and periodontitis (Jousimies-Sommer et al. 2003). Some virulence factors are known, e.g., *Porphyromonas gingivalis* has a protease and hemolysin; furthermore, lipopolysaccharides (LPS) and a capsule; *Prevotella* spp. has a protease; *Fusobacterium necrophorum* harbors a leukotoxin, hemolysin, LPS, phospholipase, and a protease; *Fusobacterium nucleatum* has a LPS, a protease and a leukotoxin (Tzianabos and Kaspar 2005). Those pathogenic factors are mainly investigated in context of the pathological pictures of the teeth, but may of course also be involved in the pathogenesis of osteomyelitis of the jaws.

7.4 Microbiological Procedures for Detection of Bacteria Found in Osteomyelitis of the Jaws

Appropriate collection and transportation of specimens are essential for accurate recovery of relevant bacteria. In general, bacterial cultures should be obtained using tissue specimens rather than swabs, as swab cultures of pus and putride exudate often contain mostly dead microorganisms. The number of microorganisms, however, must be sufficient to develop a colony growth on the culture plates. The critical number is not known, but the use of tissue specimens, which contain vastly greater numbers of viable microorganisms, is preferred (Marx 1991).

Aspirates from the adjacent soft tissue swellings may be valuable, but cultures from the sinus tracts may be misleading, because these sinus tracts are often colonized by organisms that do not reflect what is actually occurring within the infected bone. Aspiration and drainage as well as collection of representative deep tissue samples via the external skin surface provides the preferred specimen, despite the disadvantages of an external surgical approach. If the oral cavity mucous membranes must be entered, the site should be isolated with cotton rolls, dried, and swabbed vigorously with povidone–iodine, which is allowed to remain on the site for at least 1 min before the needle is inserted. Deep liquid samples must be injected into an anaerobic transport vial through a rubber septum without introducing air; the liquid should be injected slowly to ensure that specimen remains on top of agar. Because acute and especially secondary chronic osteomyelitis of the jaws is associated with anaerobes in a polymicrobic mixture, culture specimens must be sent to the microbiology laboratory immediately. Specimens cultured with as little as a 15-min delay may fail to yield certain anaerobes that can be identified in an immediate culture. The acceptable time delay when aerobic transfer media is somewhat longer, but loss of certain aerobes can occur within as little as 2 h (Marx 1991). Biopsies should be transported in a sterile tube. If the transport is delayed, a small amount of sterile physiological saline solution can be added. When no other specimen can be obtained, swabs must be transported in an anaerobic transport agar tube (Jousimies-Somer et al. 2002).

In cases of primary chronic osteomyelitis or secondary chronic osteomyelitis with predominantly sclerosing, pus and sequestration is missing; hence, a bone biopsy is of utmost importance for detection of a possible pathogen. To avoid contamination bone biopsy specimens should be harvested following a strict protocol, although an external approach, as mentioned above, would be the preferred approach from the microbiological point of view; however, harvesting bone from the mandible by an extraoral approach is surgical more demanding than from an enoral approach and harbors several complications, especially scar formation and possible facial nerve palsy. A suggested protocol is listed in Table 7.2.

Specimens must be protected from the deleterious effects of oxygen until they can be cultured. In a proper anaerobic transport medium, anaerobic bacteria may survive for up to several days. Anaerobes survive well in pieces of tissue, especially larger ones. Specimens should be transported and held at room temperature; incubator temperatures will cause differential bacterial overgrowth or loss of some strains and cold temperatures will allow increased oxygen diffusion. Because of the fastidious and oxygen-sensitive nature of many oral anaerobes, prompt processing after opening the transport vials is essential to obtaining clinically relevant re-

Table 7.2 Principles for bone biopsy for microbiological assessment of osteomyelitis of the jaws (Modified after Eyrich et al. 1999; Marx et al. 1996)

Avoidance of an extraoral approach to avoid possible nerve palsy (VII) and scar formation
Avoidance of possible contamination using an intraoral approach: – Mucous membranes must be isolated with cotton rolls, dried, and swabbed vigorously with povidone-iodine, which is allowed to remain on the site for at least 1 minute before incision of the mucosa – Use of a trepan-bur to cut out a bone cylinder off from the infected bone – Harvest only the collected bone material at the tip of the bur for microbiological culturing
Tissue specimens collected should be transported and cultured under anaerobic conditions

sults (Jousimies-Somer et al. 2002). Organisms do not grow well in bone and proper handling of specimens is important. Hand-carrying the specimen to the laboratory and requesting that bone specimens be ground or minced may increase the culture yield.

A well-prepared and properly interpreted Gram stain is a simple and rapid method to give preliminary information to the clinicians. Nonselective and selective agar plates with blood are incubated anaerobically and aerobically in 5% CO_2; a selective chocolate plate can help to find X- and V-factor-dependent hemophili. Specially suspected bacteria must be communicated to the laboratory; for the detection of *A. israelii* selective anaerobic plates must be inoculated for 10 days.

7.5 Microbiological Results in the Different Types of Osteomyelitis of the Jaws

Osteomyelitis is initiated by a contiguous focus of infection or hematogenous spread. Osteomyelitis of the jaws is caused primarily by contiguous spread of odontogenic infections originating from pulpal or periodontal tissues. Trauma, especially compound fractures, is the second leading cause of jaw osteomyelitis. Infections derived from periostitis after gingival ulceration, infected lymph nodes or hematogenous origin account for an additional small number of jaw infections. The mandible resembles long bones: it has a medullary cavity, dense cortical plates, and a well-defined periosteum; the regions affected, in decreasing frequency, are the body, symphysis, angle, ramus, and condyle. Osteomyelitis of the maxilla is much less frequent than that of the mandible because the maxillary blood supply is more extensive. Thin cortical plates and a relative paucity of medullary tissues in the maxilla preclude confinement of infections within bone and permit the dissipation of edema and pus into the soft tissues and paranasal sinuses (Topazian 2002).

Given the frequency and severity of odontogenic infections and the intimate relationship of the root ends of teeth to the medullary cavity, the relative infrequency of osteomyelitis of the jaws is remarkable. In addition to the virulence of microorganisms, conditions affecting host resistance and alteration of jaw vascularity are important in the onset and severity of osteomyelitis. Osteomyelitis has been associated with diabetes, autoimmune disease, agranulocytosis, leukemia, severe anemia, malnutrition, syphilis, cancer chemotherapy, steroid drug use, sickle cell disease, and acquired immunodeficiency syndrome (Topazian 2002). A more detailed description of the pathophysiology of jawbone osteomyelitis is described in Chap. 2.

In a study by Baltensperger (2003) 290 osteomyelitis cases involving the jaws were recorded over 30 years. In 251 of these cases, osteomyelitis with suppuration or formation of a fistula and/or sequester, representing a true bacterial infection, was the most common form described. The vast majority (203 cases or 70%) of these cases were secondary chronic osteomyelitis; 48 cases (16.6%) were classified as acute osteomyelitis and the diagnosis of primary chronic osteomyelitis was made in 30 cases; 9 cases could not be classified (Baltensperger 2003). The microbiological results of the different types of osteomyelitis are described in the following chapters and some special aspects specific infections are included.

7.5.1 Acute Osteomyelitis

In the past, osteomyelitis of the jaws, like that of the long bones, was believed to be caused primarily by the skin bacteria *S. aureus* and *Staphylococcus epidermidis*. Staphylococci can be iatrogenically introduced into the

deeper tissue planes by surgery or trauma resulting in an infectious process. Because of the plethora of microbial flora associated with the dentition and supporting tissues, and the inherent opportunity for access beneath the mucosal barrier, a large variety of organisms can act as responsible pathogens for osteomyelitis of the jaws (Hudson 1993). A decrease in the percentage of *S. aureus* osteomyelitis in recent reports is attributable to the use of more sophisticated culture methods that result in more accurate identification of responsible organisms. The previous estimate of anaerobic involvement for all instances of osteomyelitis was <1%. The number of sterile cultures from many series of patients with osteomyelitis was significant. Conversely, anaerobes now are associated frequently with aerobic organisms in osteomyelitis, and anerobic osteomyelitis also may occur alone. Findings helpful in recognition of pure anaerobic or mixed aerobic–anaerobic infections in osteomyelitis of the jaws are presence of a foul-smelling exudate, sloughing of necrotic tissue, gas in soft tissues, black discharge from the wound, Gram stain revealing multiple organisms of different morphological characteristics, failure to grow organisms from clinical specimens, particularly when Gram-negative organisms are seen on the smear, and presence of sequestra (Topazian 2002). Osteomyelitis of the jaws now is recognized as a disease caused primarily by viridans streptococci and oral anaerobes, particularly *Peptostreptococcus* spp., *Fusobacterium* spp., and *Prevotella* spp., the organisms responsible for odontogenic infections (Topazian 2002). This picture can change markedly over time as the infectious process matures and isolates itself from the host defense mechanisms (Hudson 1993). A few organisms apparently are derived from perimandibular space infections that also may involve *E. corrodens* in a relatively high percentage of patients (Peterson and Thomson 1999). Mixed bacterial cultures, hemolytic streptococci, pneumococci, typhoid and acid-fast bacilli, *Escherichia coli*, and *Actinomyces* spp. account for the remaining infections.

In the retrospective analysis by Baltensperger (2003), microbiology specimens were collected from deep wound or pus in 29, and from the bone in 5 of 48 cases of acute osteomyelitis. In almost all cases, miscellaneous anaerobic bacterial flora was identified with viridans streptococci being by far the predominant isolated bacteria. Half of the viridans streptococci were further specified to be in the *S. milleri* group. In two bone specimens and in five specimens from deep wound and/or pus bacteria normally found infrequently in the oral cavity, were isolated, i.e., *E. coli* (*n*=2), *Enterobacter* spp. (*n*=2), *Klebsiella* spp. (*n*=1), *Serratia* spp. (*n*=1), and *Proteus* spp. (*n*=1). Enteric bacteria in osteomyelitis of the mandible were also recently described in two patients (Scolozzi et al. 2005). *S. aureus* was only found in 3 cases and coagulase-negative staphylococci in 5 cases (Baltensperger 2003).

In a older overview of 60 cases of osteomyelitis of the mandible, 15 had posttraumatic osteomyelitis, 4 had postoperative osteomyelitis, 13 had odontogenic osteomyelitis, and 28 had osteoradionecrosis. In most infections (93%) polymicrobial (average, 3.9 organisms per patient) and anaerobes played an important role. Only 3 patients' biopsy specimens yielded no organism on culture. The most common organisms isolated were *Streptococcus* spp., *Bacteroides* spp., *Lactobacillus* spp., *Eubacterium* spp., and *Klebsiella* spp. Other frequently cultured organisms included *S. aureus*, *E. coli*, *Veillonella parvula*, *Fusobacterium nucleatum*, and *Peptostreptococcus magnus* – renamed recently as *Finegoldia magna*. In addition, 4 patients' cultures yielded *Candida albicans* or *C. tropicalis*, four cultures yielded *Actinomyces* spp., and one yielded *Aspergillus* spp. Cultures from 30 of the 60 patients yielded anaerobic organisms (Calhoun et al. 1988).

7.5.2 Secondary Chronic Osteomyelitis

As a sequel of acute osteomyelitis, secondary chronic osteomyelitis shares the same etiology and pathogenesis as the acute form; hence, the usual cause of secondary chronic osteomyelitis of the jaws is also bacterial invasion from a contagious focus. Most frequent sources are odontogenic foci, periodontal diseases and pulpal infections, extraction wounds, and infected fractures. Prolongation of the bone infection is a result of the inability of the host to eradicate the pathogen due to lack of or inadequate treatment.

In the analysis by Baltensperger (2003), microbiology specimens from bone were obtained in 46 of 203 patients and from deep wound or pus in 96 patients. Similarly to cases of acute osteomyelitis, bacteria from the miscellaneous anaerobic flora were identified in almost all instances. Viridans streptococci were identified from 21 bone samples and from 54 wound and pus samples; half of them were identified as *S. milleri* group which is frequently found together with miscellaneous anaerobic flora in oral abscesses. *Hemophilus* spp. and *Actinomyces* spp. were both isolated in 15 cases and *Candida albicans* in 5 cases. In 17 specimens *Enterobacteriaceae*, e.g., *E. coli* were isolated. *Mycobacterium tuberculosis*

was found in one case. *S. aureus* was found in two bone samples and ten samples from wound or pus samples. Coagulase-negative staphylococci were isolated in one third of the samples (Baltensperger 2003).

Actinomyces spp. and other fastidious organisms, such as *E. corrodens*, are known as pathogens in some of the more refractory forms of osteomyelitis of the jaws. These organisms are contaminants with the original odontogenic microorganism invasion, but only become established after suboptimal therapeutics failed to eradicate all potential pathogens (Hudson 1993).

7.5.3 Actinomycosis, Nocardial Osteomyelitis of the Jaws, and Special Situations

In addition to the bacteria normally found in the oral cavity, *M. tuberculosis*, *Treponema pallidum*, *Brucella* spp., and *Salmonella* spp. have been described to cause acute and secondary chronic osteomyelitis of the jaws in rare instances. The essential forms of osteomyelitis by *Actinomyces* spp. and *Nocardia* spp. are described in this chapter. Furthermore, special clinical situations, such as osteomyelitis of the jaws in newborns, infants and immunosuppressed children, as well as osteomyelitis of the jaws during pregnancy and after Lemierre syndrome, are mentioned below.

Acute osteomyelitis of the maxilla in the newborn is a rare infective condition of the maxilla which subsequently spreads to include the eye as well as the nasal and oral cavities with their attending signs and symptoms. The organism responsible is usually *S. aureus* and early diagnosis and treatment can result in rapid resolution of the condition (Loh and Ling 1993). Infection may reach bone as a result of local trauma of the overlying mucosa of the alveolar ridges, local injury to bone, extension of infection from adjacent teeth or soft tissues, and hematogenous spread from distant sources. Osteomyelitis of the jaws in infants is an uncommon disease but merits special mention because of the risks of involvement of the eye, extension to the dural sinuses, and the potential for facial deformities and loss of teeth resulting from delayed or inappropriate treatment (Topazian 2002). (A typical case of acute osteomyelitis in a newborn is described in Chap. 12).

Osteomyelitis of the jaws in children on immunosuppressive chemotherapy may need special microbiological investigations. An immunosuppressed child presenting with local swelling loss of teeth, and not responding to broad-spectrum antibiotic medication, constitutes a major clinical problem. Opportunistic osteomyelitis in the jaws with *Apergillus flavus*, *Saccharomyces cerevisiae*, and *Actinomyces* spp. have been described in children undergoing chemotherapy. Treatment was radical surgery to remove all infected and necrotic tissue. It is necessary to diagnose specific agents. A wide variety of opportunistic pathogens can cause infections in immunodeficient hosts (Hovi et al. 1995).

Osteomyelitis of the mandible during pregnancy is a rare situation, a single case without microbiological investigations has been described (Clover et al. 2005).

Osteomyelitis of the jaw can also be a complication of the Lemierre syndrome. Odontogenic infections that generally originate from infected or necrotic pulp may spread to fascial spaces of the lower head and upper neck. The predominant organisms recovered from deep facial infections are *S. aureus* and group A streptococci and anaerobic bacteria of oral origin mixed with aerobic bacteria (Brook 2003).

7.5.3.1 Actinomycotic Osteomyelitis of the Jaws

Actinomycosis is a chronic, slowly progressive infection with both granulomatous and suppurative features; it usually affects soft tissue and, only occasionally, bone. It forms external sinuses that discharge distinctive sulfur granules and spreads unimpeded by anatomical barriers when endogenous oral commensals invade the tissues of the oral-cervicofacial, thoracic, pelvic, and abdominal (ileocecal) regions. Tissues may be invaded by direct extension or by hematogenous spread. About two thirds of cases are cervicofacial. Cervicofacial disease may affect the mandible and overlying soft tissues, parotid gland, tongue, and maxillary sinuses (Topazian 2002).

A. israelii is mostly responsible for the human actinomycosis. *A. naeslundii*, *A. odontolyticus*, and *A. meyeri* are less common causes of the disease. Most infections are accompanied by other organisms, such as *A. actinomycetemcomitans*, *Bacteroides* spp., *E. corrodens*, *Enterobacteriaceae*, *Fusobacterium* spp., *Porphyromonas* spp., *Prevotella* spp., staphylocci, and streptococci, and may be potential copathogens that aid in the inhibition of host defenses or reduce oxygen tension (Russo 2005). *Actinomyces* spp. are Gram-positive, non-spore-forming, non-acid-fast bacteria; *A. israelii* and *A. meyeri* are strictly anaerobic bacteria, wheras the other *Actinomyces* spp. can grow aerobically. *Actinomyces* spp. are not highly virulent pathogens but are endogenous oral saprophytes present in periodontal pockets, carious teeth, and tonsillar crypts that take advantage of infection, trauma, or surgical injury to penetrate normal intact mucosal barriers and invade adjacent tissues. When

actinomycosis occurs, it is certain to be endogenous in origin. Although the disease has been connected with steroid use and chemotherapy, lung and renal transplantation, renal failure, metastatic carcinoma, and HIV infection, *Actinomyces* are rarely opportunistic in compromised hosts (Russo 2005).

Diagnosis is based on culture or biopsy of the lesion. Initially aspiration of a specimen for a Gram-stain smear and antimicrobial sensitivity testing for aerobic and anaerobic organisms is imperative. In actinomycosis the smear reveals Gram-positive organisms of various morphological types, particularly diphtheroid and filamentous forms (Topazian 2002). Specific immunofluorescent staining to distinguish among the various species of actinomycosis is available (Holmberg 1987; Lambert et al. 1967).

Tissue specimens should be taken to the microbiology laboratory and cultured immediately, without delay in the office or operation theater. The tissue should further also be submitted for microscopic examination and Gram staining, as *Actinomyces* spp. are Gram positive and easily identifiable on smears or within tissue preparation, even with hematoxylin and eosin staining (Fig. 7.1; Marx 1991)

7.5.3.2 Nocardial Osteomyelitis of the Jaws

Nocardiosis is a chronic disease that resembles actinomycosis. Although it occurs primarily in the lungs, from which it may spread hematogenously to the nervous system and soft tissues, it occasionally involves the cervicofacial region involving bone. Human disease usually is caused by *Nocardia asteroides*, an aerobic, delicate, Gram-positive, beaded, branching filamentous, variably acid-fast organism. Human nocardiosis also is caused by *Nocardia farcinica*, *Nocardia brasiliensis*, *Nocardia nova*, *Nocardia transvalensis*, and *Nocardia otitiscaviarum*. It is a soil saprophyte and usually gains access to the body through inhalation or by direct inoculation of skin or soft tissues. It is not a normal oral inhabitant. Although nocardiosis occurs as an opportunistic infection in compromised hosts, it may be seen also in apparently healthy individuals. In the jaws it may occur with or without dental injury and forms suppurative lesions with acute necrosis and abscess formation (Topazian 2002).

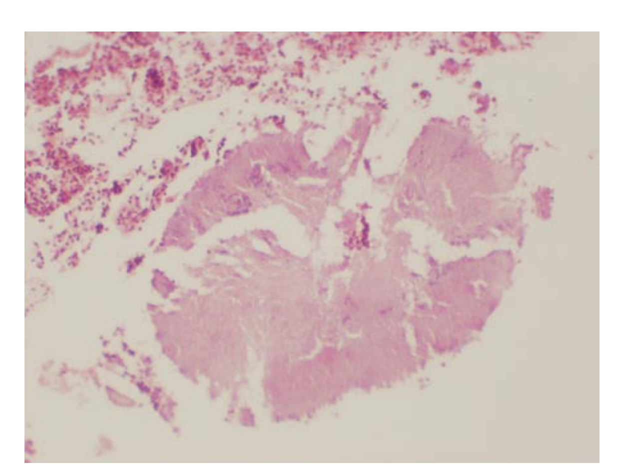


Fig. 7.1 Microscopic view of a “sulfur granule” shows a colony of *Actinomyces* surrounded by polymorphonuclear leukocytes (Hematoxylin and eosin stain; original magnification ×400)

7.5.4 Primary Chronic Osteomyelitis

Primary chronic osteomyelitis of the jaws is a rare, nonsuppurative, chronic inflammatory disease of unknown etiology. In 21 of 30 bone specimens from patients with primary chronic osteomyelitis, taken during surgery for microbiological investigations, miscellaneous anaerobic bacterial flora and viridans streptococci were predominately isolated. Coagulase-negative staphylococci were isolated from eight cultures (Baltensperger et al. 2004). In a subset of those patients with primary chronic osteomyelitis of the jaw associated with synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO syndrome) mixed aerobic and anaerobic bacteria were isolated (Eyrich et al. 1999). *Propionibacterium acnes* was also the only infectious agent isolated from osteoarticular lesions in patients with SAPHO syndrome in another study (Kahn et al. 1994). Besides *P. acnes*, also *Actinomyces* spp. and *E. corrodens* have been detected from a large number of biopsy specimens in a prospective study by Marx et al. (1994). Microbiological specimens taken from the bone revealed predominantly normal endogenous oral bacteria. Because all biopsy samples were collected via intraoral approach, lacking a special protocol, these results were considered as contaminations (Eyrich et al. 2003).

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Osteomyelitis Therapy – General Considerations and Surgical Therapy

Marc Baltensperger and Gerold Eyrich

8

Contents

8.1 Summary

The final common pathway in all treatment of acute and secondary chronic osteomyelitis of the jaws is to achieve a shift in the disturbed balance between the responsible pathogen(s) and host defenses to the latter, allowing the body to overcome the infection. Reduction of pathogens is achieved by surgical removal of infected and necrotic tissue as well as by antibiotic therapy. Improvement of local vascularization is further accomplished by surgical decortication, exceeding conventional surgical debridement, which not only removes the poorly vascularized (infected) bone but also brings well-vascularized tissue to the affected bone, thus facilitating the healing process and allowing antibiotics to reach the target area; therefore, surgery and antibiotics are to be considered the major columns in treating osteomyelitis of the jaws.

Hyperbaric oxygen (HBO), which can be recognized as an adjunctive therapeutic modality in treatment of acute and secondary chronic osteomyelitis, supports host-defensive mechanisms and promotes tissue vascularization as well as has direct toxic effects on microorganisms causing the infection. Although never as dominating as surgery and antibiotic therapy, HBO is to be considered the third column in the armentarium for acute and secondary chronic osteomyelitis treatment.

A sufficient surgical debridement is as the most important factor in successful treatment of advanced acute and secondary chronic osteomyelitis of the jaws. The extent of the surgical debridement is dictated mainly by the extent of the infected bone. The most important surgical procedure to achieve a sufficient debridement and in addition bring well-perfused tissue in contact with the surgical site is the decortication procedure, which is considered the workhorse in surgical treatment of acute and secondary chronic osteomyelitis of the jaws.

The main goal in treatment of primary chronic osteomyelitis of the jawbone is cessation or amelioration of symptoms. In addition, bone deformity may or must be surgically addressed. Dealing with symptoms, aside from surgery, several conservative treatment options are available. Even though the disease may not been cured, change of course and severity should be considered a sign of success.

8.2 General Aspects of Osteomyelitis Therapy

Until the mid-twentieth century, the treatment of osteomyelitis of the jaws, like osteomyelitis of long bones in

other parts of the skeleton had been primarily surgical. Back then, osteomyelitis of the jaws was an infectious disease with an often complicated course, involving multiple surgical interventions and not seldom leading to facial disfigurement as a result of loss of affected bone and teeth and the accompanying scarring. The outcome was usually all but certain and hence prolonged treatment and frequent relapses have been associated with this disease in the past; however, since the second half of the past century there has been a dramatic reduction of the incidence of osteomyelitis cases involving the jaws and other bones of the skeleton (Hudson 1993). The major responsible factor leading to this development must probably be seen in the introduction of antibiotics to the therapeutic armamentarium; however, other factors have also contributed to this fact such as improved nutrition, and better availability to medical and dental care, especially including advances in preventive dentistry and oral hygiene. Earlier diagnosis due to more sophisticated diagnostic imaging modalities has additionally improved the morbidity associated with this disease (Hudson 1993; Topazian 2002).

Current treatment of osteomyelitis of the jaws usually consists of a combination of surgical and antibiotic therapy. Hyperbaric oxygen (HBO) has been established for treatment and prevention of osteoradionecrosis with good scientific documentation of its therapeutic value for this indication (Marx 1983, 1999; Marx and Johnson 1986; Marx et al. 1985); however, the role of adjunctive HBO in the treatment of osteomyelitis of the jaws has to date not been well defined, and hard scientific evidence of its therapeutic value is still lacking. Indeed, in acute and secondary chronic osteomyelitis of the jaws, HBO is usually less frequently required than in cases affecting the long bones and other parts of the skeleton, because of the greater vascularity of the head and neck (Marx 1991). In general, in most cases of acute and secondary chronic osteomyelitis of the jaws, resolution is attainable without HBO. Despite the aforementioned information, clinical experience shows the adjunctive use of HBO beneficial in cases proved refractory to surgical and antibiotic therapy and in patients who are seriously medically compromised with no HBO contraindications (Marx 1991; Topazian 2002). According to Marx (1991) the indication to add HBO to a protocol for treatment of secondary chronic osteomyelitis of the jaws requires three conditions: (1) the disease has been refractory to treatment for at least 1 month after adequate surgical debridement/decortication; (2) antibiotic treatment has been culture directed; and (3) no further focus of infection has been discovered. In some cases of acute osteomyelitis antibiotic therapy with or without adjunctive HBO may be successful, and major surgical intervention can be avoided (Baltensperger 2001).

An in-depth description of use of antibiotic therapy and HBO in treatment of osteomyelitis of the jaws are given in Chaps. 9 and 10.

This chapter first focuses on general and surgical aspects of therapy of acute and secondary chronic osteomyelitis of the jaws. Therapy of these two types of osteomyelitis is similar, since etiology and pathogenesis are identical in both. Therapy of primary chronic osteomyelitis is more difficult compared with acute and secondary chronic cases, because of lack of knowledge of the exact etiology and pathogenesis of this disease to date. It is discussed more extensively later in this chapter.

8.2.1 Principles of Therapy of Acute and Secondary Chronic Osteomyelitis

The final common pathway in all treatment of acute and secondary chronic osteomyelitis of the jaws is to achieve a shift in the disturbed balance between the responsible pathogen(s) and host defenses to the latter, allowing the body to overcome the infection. This is primarily achieved by reduction of the pathogens by number and, on the other hand, by increasing host defense mechanisms and local tissue perfusion (Fig. 8.1). These goals are mainly achieved by surgery and antibiotics which are considered the major pillars in treatment of osteomyelitis of the jaws (Fig. 8.2). Reduction of the number of pathogens is the main effect of antibiotic therapy. Besides reducing the number of pathogens by removal of infected and necrotic tissue, surgical therapy furthermore brings well-perfused tissue to the affected area.

Despite the abovementioned limitations, HBO may be seen as a third pillar in treatment of acute and secondary chronic osteomyelitis (Fig. 8.2). Its mechanisms in osteomyelitis therapy are to reverse the hypoxic state of the infected bone, enhancing leukocyte killing potential as well as its direct toxic effect on strict anaerobes and facultative anaerobes. Furthermore, HBO promotes angiogenesis in the tissue and hence increasing local tissue perfusion (Marx 1991).

From the clinician's point of view the goals in treatment of acute and secondary chronic osteomyelitis are more or less the same (Table 8.1). Due to the different time frame for establishment of the bone infection, the disease is usually more advanced in cases of secondary chronic osteomyelitis. On the other hand, symptoms such as pain and patients discomfort may be more prom-

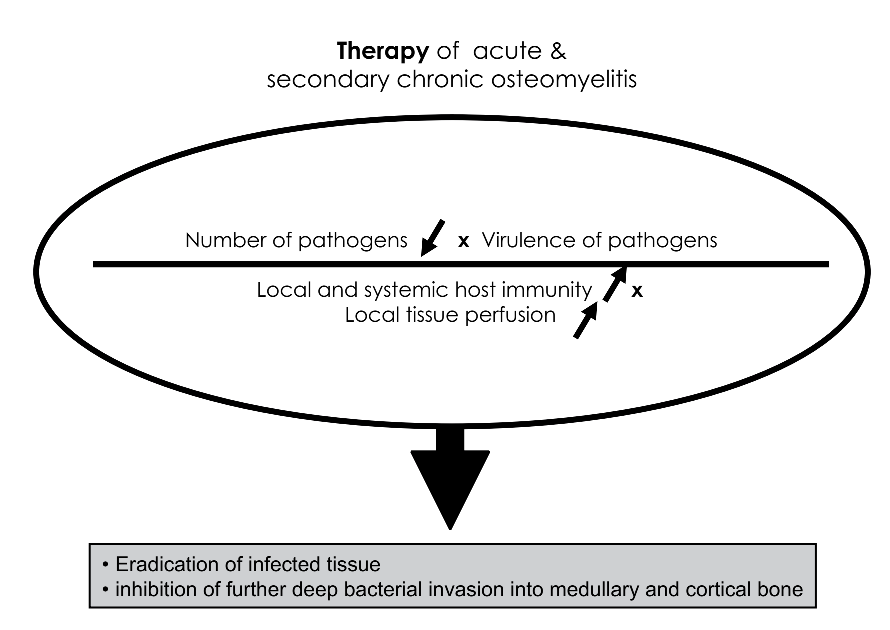


Fig. 8.1 Mechanisms in treatment of acute and secondary chronic osteomyelitis of the jaws

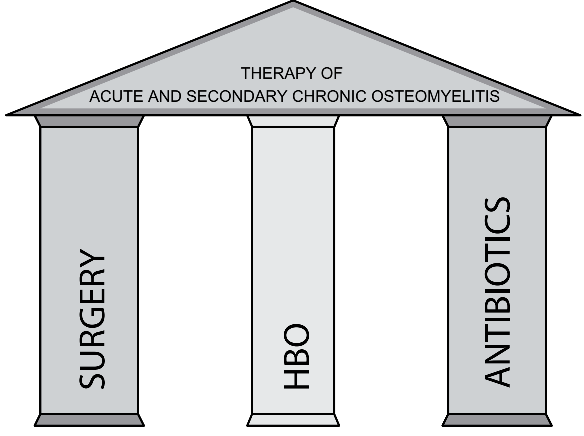


Fig. 8.2 The major columns of acute and secondary osteomyelitis therapy

Table 8.1 Therapeutic goals in treatment of acute and secondary chronic osteomyelitis of the jaws

Eradication of infection and removal of infectious focus
Pain management
Limitation of further spreading of the disease
Fracture prophylaxis, and stabilization of infected fractures
Preservation of anatomic structures when possible
Prevention of relapse of disease
Prevention of (further) chronification of the infection
Reestablishment of anatomy and function

inent in acute cases, as described extensively in Chap. 2. For these reasons therapy and management of acute and secondary chronic osteomyelitis of the jaws may differ.

8.2.1.1 Acute Osteomyelitis

Prior to successful treatment of any disease is the establishment of a correct diagnosis. According to the hierarchic order of classification criteria mentioned in Chap. 2 (Table 2.7), the clinical picture and imaging studies are the most important tools in diagnosis of jawbone osteomyelitis.

As discussed in Chap. 2, vascular compromise caused by the infective process occurs early in the course of the disease, making a cure unlikely unless medical management of acute osteomyelitis of the mandible with an appropriate antibiotic is instituted within the first 3 days after onset of symptoms. This requires early detection of the disease from the patient's history and medical exams (Mercuri 1991). Radiological imaging, as described extensively in Chap. 3, with conventional films, CT, and possibly MRI, is necessary to confirm the suspected diagnosis and define the extent of the lesion. Radionuclide scans may be necessary to confirm the infection in these



early stages when other imaging studies are still negative and of limited diagnostic value.

Removal of the cause, usually a dental focus, local incision, and drainage of pus and occasionally local curettage with removal of superficial sequestra, foreign bodies/implants and saucerization are necessary to ensure an environment for healing. These procedures lead to decompression of acute intramedullary and subperiosteal osteomyelitis of the jaws and are essential for the prevention of further vascular and cortical compression, resulting in necrosis of bone and soft tissue and progression of the disease (Mercuri 1991). Specimens for Gram stain, culture, and sensitivity testing are harvested as well during these initial procedures. Furthermore, histopathological examination may be done to confirm the diagnosis and rule out other pathology (e.g., malignancy) in unclear cases.

If an underlying host defense deficiency exists, this requires immediate attention and correction if possible, preferably prior to surgical intervention. Factors compromising local tissue perfusion must be recognized, since they will strongly influence therapy and the course of the disease. It is important that these factors be identified and addressed early in the course of therapy if treatment is to be successful. Consultation with the appropriate medical specialist will be helpful in resolving many of these underlying problems (Mercuri 1991).

Antibiotic therapy is usually started empirically with a broad-spectrum antibiotic and adapted to a more specific culture-guided therapy, if necessary, as soon as possible.

Whenever possible, specimens should be obtained for Gram staining, aerobic and anaerobic cultures, as well as for antibiotic sensitivity testing. Appropriate mucosal and skin preparation is vital in specimen collection. Sterile, large-gauge needles should be used to aspirate areas of suspected pus deposits. Material removed by debridement should be transported and cultured under anaerobic conditions (Fig. 8.2; see also Chap. 7). Gram stains may be helpful to determine initial antibiotic therapy until laboratory results are available. The consistency, color, and odor of pus may provide important clues to initial diagnosis and treatment. For example, thick creamy pus from a localized abscess is indicative for a staphylococcal infection. A foul-smelling, dark exudate accompanying slough of necrotic tissues, gas in soft tissues, and multiple organisms in Gram stain of variable morphological characteristics strongly suggests anaerobic osteomyelitis (Topazian 2002); however, the limitations of microbiological investigations in osteomyelitis of the jaws must be respected when interpreting these results, due to possible contamination of the collected specimen (see Chap. 7).

If the infection does not respond adequately, the regime must be questioned and adjustments must be made, including repeated cultures to ensure correct antibiotic therapy, more extensive surgical debridement (e.g., decortication, resection) and possibly adjunctive HBO therapy. The principles of treatment of acute osteomyelitis of the jaws are given in Table 8.2.

8.2.1.2 Secondary Chronic Osteomyelitis

As stated previously, the principles of therapy and management of secondary chronic osteomyelitis are similar to those in cases of acute osteomyelitis and yet differ somewhat due the usually larger extent of the established chronic infection. Because the infection is, by definition, more advanced than in acute cases, radiological imaging is usually more conclusive. Clinical symptoms, on the other , may be less or more prominent than in cases of acute osteomyelitis.

The principles in treating cases of secondary chronic osteomyelitis of the jaws is basically the same, regardless of whether the course is chronic suppurative or more a diffuse sclerosing character (Table 8.3).

Initial correct diagnosis of secondary chronic osteomyelitis must be established prior to any successful treatment. Adequate diagnosis can usually be achieved based on history, clinical evaluation, and imaging studies. Diagnostic imaging (e.g., CT scans) are considered the gold standard in determining the extent of the lesion prior to surgery (see also Chap. 3). In special situations when an underlying malignancy is suspected, a biopsy procedure prior to the actual surgical intervention is advisable.

Initial therapy of secondary chronic osteomyelitis of the jaws starts with an adequate surgical debridement which is mainly dictated by the extent of the infection. Adequate means removal of the initial source of the infection, if still present as well as foreign bodies/implants and nonviable tissues included in the infectious process.

Ideally, antibiotic treatment should be withheld prior to, and even during, surgery until culture specimens have been obtained. Once all specimens are collected, empiric antibiotic treatment can be initiated; however, in daily practice, many cases of secondary chronic osteomyelitis of jaws have already been pretreated with antibiotics by the referring physician.

The principles for collecting specimens are the same as described earlier in this chapter as well as extensively

Table 8.2 Principles of treatment of acute osteomyelitis of the jaws

Establish correct diagnosis, based on history, clinical evaluation, and imaging studies
Biopsy in unclear cases to rule out other pathology (e.g., malignancy)
Determine extent of infected bone and soft tissue
Evaluation and correction of host defense deficiencies when possible
Removal of source of infection, usually a dental focus, foreign bodies/implants
Local incision and drainage of pus
Local curettage with removal of superficial sequestra and saucerization if necessary
Collection of specimens for Gram stain, culture and sensitivity, histopathology
Begin with empiric broad-spectrum antibiotic therapy and change to culture-guided antibiotics as soon as possible
More extensive surgical debridement if necessary (e.g., decortication, resection)
Possible adjunctive hyperbaric oxygen therapy

Table 8.3 Principles of treatment of secondary chronic osteomyelitis of the jaws

Establish correct diagnosis, based on history, clinical evaluation, and imaging studies
Biopsy in unclear cases to rule out other pathology (e.g., malignancy)
Determine extent of infected bone and soft tissue
Evaluation and correction of host defense deficiencies when possible
Surgical debridement of infected tissue dictated by extent of the lesion (removal of affected teeth and foreign bodies/implants, sequestrectomy, local curettage, saucerization, decortication, resection)
Collection of specimens for Gram stain, culture and sensitivity, histopathology
Begin with empiric broad-spectrum antibiotic therapy and change to culture-guided antibiotics as soon as possible
Possible adjunctive hyperbaric oxygen therapy
More extensive surgical debridement if necessary (e.g., repeated decortication, resection)

in Chap. 7. It must be emphasized that tissue samples are more reliable for obtaining reliable cultures than swabs, as swab cultures of pus or putrid exudate often contain mostly dead microorganisms (Marx 1991).

After surgical debridement, high-dose antibiotic therapy is then initiated at frequent intervals. As in cases of acute osteomyelitis, the initial antibiotic management of secondary chronic osteomyelitis of the jaws is at this stage empiric, but choices should be based on such clinical observations at the time of surgery as color, odor, and consistency of pus and tissue. In general, initial antibiotic therapy will consist of a broad-spectrum drug with a low toxicity and bactericidal character. Adjustments are made as soon as sufficient culture data is available.

Patients with osteomyelitis usually require treatment as in-patients. In our review most patients diagnosed primarily with acute or secondary chronic osteomyelitis were hospitalized at some point during their treatment. Only in few instances was treatment conducted

on solely an out-patient basis (Baltensperger 2003). Repeated hospitalizations were seldom required, except for complicated cases involving repeated surgical procedures. Furthermore, the use of HBO extended inpatient therapy in some instances when the patient lived far from the university medical center.

The end point of the antibiotic therapy in acute and chronic osteomyelitis of the jaws is usually based on empiric judgment and is guided by clinical and possible follow-up imaging studies. Cessation of suppuration, adequate healing of the surgical wound, full regression of the cardinal signs of infection (e.g., calor, rubor, dolor, tumor, and impaired function) are important signs for which to look. Imaging should demonstrate cessation of osteolysis and sequester and some early bone remodeling. In general, antibiotic therapy may therefore be extended for a period of 4–6 weeks after surgery. General and specific principles of antibiotic therapy in jawbone osteomyelitis are discussed in extent in Chap. 9.

In cases of persistent infection, despite the abovementioned therapy, adjunctive HBO and possibly further surgical debridement must be evaluated. The principles of treatment of secondary chronic osteomyelitis of the jaws are given in Table 8.3.

8.2.1.2.1 Secondary Chronic Osteomyelitis Associated with Bone Pathology and/or Systemic Disease

Of all types of secondary chronic osteomyelitis of the jaws, cases associated with a local or systemic bone pathology and/or a systemic disease deserve to be mentioned separately because the underlying pathology facilitating osteomyelitis has a great impact on therapy.

8.2.1.2.2 Secondary Chronic Osteomyelitis Associated with Bone Pathology

In general, bone pathology altering metabolism and vascularization facilitates the inoculation and spreading of microorganisms and thus helps establishment of the infection. Since host defenses are usually impaired in cases of underlying bone pathology, physiological bone reactions, such as neoosteogenesis, periostitis, and sequester formation, which are the result of osteoblastic and osteoclastic activity, may be less prominent or even absent in these cases; thus, diagnosis can be challenging.

Preferably concomitant pathology facilitating infection is addressed as early as possible in the therapeutic process. In cases of underlying bone pathology this is not possible. Principally, it must be differentiated between a localized and generalized, systemic bone pathology. This differentiation has a big impact on the proposed surgical therapy. In cases of localized bone pathology surgical therapy may be more extensive, including not only the infected bone but extending surgery to regions of vital bone which are not affected by the infection and the underlying bone pathology. Antibiotic therapy may be less effective since local vascularization may be diminished, hindering establishment of sufficient concentration in the target area.

A typical example for this type of localized bone pathology is infected osteoradionecrosis. Radiation to the jaws exceeding a dosage of 50 Gy kills bone cells and results in a progressive obliterative arteritis (endarteritis, periarthritis, hyalinization, and fibrosis and thrombosis of vessels). All periosteal vessels as well as larger vessels, such as the inferior alveolar artery, are affected markedly, resulting in compromised vascularity or aseptic necrosis of the bone in severe cases. As long as the overlying soft tissues do not break down, irradiated bone may survive (Topazian 2002); however, if trauma or other factors lead to exposure of the bone to the oral cavity, contamination and possible subsequent invasion of microorganisms into the bone may result. Surgical therapy in these cases most usually includes resection not only of the infected bone but also the severely radiated bone tissue. Hyperbaric oxygen therapy is also helpful in these instances to increase bone vascularization in and hence may help limiting resection. Microvascular tissue transfer is usually required to repair the resulting surgical defect. Specific procedures are well described in textbooks of head and neck surgery and are beyond the scope of this book.

If the underlying bone pathology is of systemic nature, a different therapeutic approach is necessary since all bone is potentially affected by this condition. A typical representative of this group is osteonecrosis or osteochemonecrosis caused by bisphosphonate therapy. This condition, also described as bis-phossy jaw, has become strikingly more prominent in recent years. Although historically other medications, such as corticosteroids and chemotherapy, have also been attributed to osteochemonecrosis of the jaw, osteochemonecrosis of the jaws caused by bisphosphonates is by far the clinically most significant to date.

The pathogenesis of osteochemonecrosis of the jaw is yet not fully understood. Current opinions suggest more of bacterial cofactor risk than osteoradionecrosis, and although altered angiogenesis may yet prove to be a

factor, avascularity does not appear to be a major cofactor (Hellenstein et al. 2005).

Bisphosphonates affect bone physiology. Especially osteoclastic activity is diminished. This alteration limits the ability of bone healing after trauma and therefore makes bone tissue more susceptible to secondary bacterial infection. Because of the reduced healing capacity of bone, surgical intervention is accompanied by a high complication rate in such instances; therefore, in cases of osteochemonecrosis of the jaw complicated by osteomyelitis, surgery should be limited to a minimal debridement of the necrotic bone and primary closure of the surgical site with a mucoperosteal flap. Extended antibiotic therapy and possibly HBO should always be considered as adjunctive therapy modalities.

For patients currently receiving bisphosphonates who require oral surgical procedures, there is no clear evidence to date that supports that interruption of bisphosphonate therapy will prevent or lower the risk of osteochemonecrosis of the jaw, however, depending on duration and mode of administration of bisphonate (e.g. intravenous or per oral), temporary cessation of bisphonate therapy (drug holiday), is currently being investigated. Regarding the rapidly increasing number of patients receiveing bisphonate therapy more distinctive guidelines regarding this question are needed and will hopefully be available in the near future.

If surgery is necessary in cases of established osteochemonecrosis, such as in instances complicated by osteomyelitis, stopping or interrupting bisphosphonate may be considered; however, close coordination between the surgeon and the priscribing physician (e.g. oncologist or other medical specialist) is recommended. Assessing the potential risk of further osteonecrosis and infection versus the risk of skeletal complications or hypercalcemia of malignancy is important and must be judged on an individual basis (Ruggerio et al. 2006).

As in patients receiving radiotherapy of the head and neck and/or chemotherapy, patients who are planned to be treated with intravenous bisphosphonates should receive a thorough dental examination prior to beginning therapy. Dental treatments and procedures that require bone healing should be completed before initiating intravenous bisphosphonate therapy, if possible. Patients should be instructed on the importance of maintaining good oral hygiene and having regular dental assessments (Ruggerio et al. 2006).

Another systemic condition with affects the bone and the jaws is osteopetrosis (Albers–Schonberg disease or marble bone disease). Osteopetrosis is a genetically inherited disease. Bones of patients suffering from this disease progressively become more mineralized and less vascular (see Fig. 2.32, Chap. 2).

Osteopetrosis affects local bone pathology by progressive reduction in perfusion and cellular content. Furthermore, gradual ossification of the medullar component of the bone leads to inhibition of marrow function resulting in anemia and leukopenia. As with other systemic pathologies affection bone as the main target tissue, osteopetrosis complicated by secondary chronic osteomyelitis of the jaws is best treated by using minimal surgical intervention whenever possible. The bone in these patients is hypovascular and hypocellular and therefore has a limited healing capacity. In addition, the poor vascularization of the osteopetrotic bone does not promote granulation tissue development or bone regeneration to progress across the defect. Surgical defects resulting from debridement cannot be reconstructed with bone grafts for all donor sites are affected with the same pathology. Antibiotics have minimal impact on the disease because of the reduced vascularity, and HBO does not have the same angiogenesis effect in osteopetrosis as that it does in osteoradionecrosis. Their adjunctive use is, therefore, targeted at the surrounding soft tissue even more than the bone in an effort to prevent further exposure of osteopetrotic bone. Complete resolution of the infection may be difficult or even impossible. The treatment of secondary chronic osteomyelitis of the jaws in patients with osteopetrosis is designed to control the disease process. Treatment is primarily composed of minimal tissue debridement, irrigations, and perhaps topical antibiotics (Marx 1991).

Malignant tumors with concomitant secondary bone infection or the rare cases of chronic osteomyelitis with malignant transformation must be addressed aggressively following principles of tumor surgery. Resection of the affected area with a secure margin and a healthy tissue is usually also a sufficient treatment of the osteomyelitis. Further management of potential infectious (dental) foci must be also focused upon regarding possible subsequent radio- and/or chemotherapy.

8.2.1.2.3 Secondary Chronic Osteomyelitis Associated with Systemic Disease

As mentioned above, systemic conditions facilitating the development and progress of acute and secondary chronic osteomyelitis (of the jaws) must be addressed as early as possible in the treatment cascade (Tables 8.2, 8.3).

Several conditions influence the ability of the patient to deal with the bone infection using different

pathophysiological mechanisms. The most common predisposing pathological conditions are covered in detail in Chap. 2. While the treatment of concomitant and predisposing pathology is beyond the scope of this book, certain direct impacts on the treatment of osteomyelitis of the jaws are the focus.

Diabetes is a widespread clinical condition. The pathophysiology of diabetes influences the development and continuation of osteomyelitis in several ways. Leukocytes of diabetic patients have a diminished chemotaxis, phagocytosis, and a reduced life span. Furthermore, diabetic micro- and macroangiopathy reduces tissue perfusion and hence the ability to mount an effective inflammatory response, and the delivery of antibiotics to the target area. Wound healing in diabetic patients is also reduced for reasons mentioned above and partly because of protein breakdown from defective glucose utilization. The sum of these mechanisms leads to a reduction of host resistance, which perpetuates infection. Treatment of osteomyelitis of the jaws in diabetic patients must therefore in general be more aggressive regarding surgical intervention, wound care, antibiotic management, and adjunctive therapy, such as HBO, in addition to control the diabetic state (Marx 1991).

Leukemia in all its forms has a strong impact on function and number of white blood cells causing a favorable condition of osteomyelitis of the jaws to develop. While the number of leukocytes is increased in the leukemia patient, the majority of these cells are poor or nonfunctional. Malignant proliferation of white blood cells within the marrow causes a crowding and jeopardizes the development of red blood cells leading to myeloplastic anemia. This condition reduces tissue oxygenation and therefore further reduces leukocyte and macrophage microbial killing ability.

Chemotherapy used for treatment of the leukemia furthermore has a general negative effect on the general healing capacity by reducing tissue integrity in general.

Treating patients with leukemia and secondary chronic osteomyelitis of the jaws starts conservatively with empiric broad-spectrum antibiotics, which should be culture guided as soon as possible. The surgical phase of the protocol in these patients should be delayed until approximately 2 weeks after chemotherapy is sustained and functional white blood cells have recovered. A close cooperation with the oncologist is necessary to coordinate treatment.

Severe anemias (e.g., sickle cell anemia) may promote acute and secondary chronic osteomyelitis of the jaws via systemic debilitation, reduced tissue oxygenation, and bone infarction. Especially predisposed anemia patients for osteomyelitis are children who are homozygous for the anemia trait (Marx 1991). Usually intensive and aggressive management of the anemia as well as the osteomyelitis is required on an inpatient setting with close cooperation of the involved medical disciplines.

Intravenous drug abusers may develop chronic osteomyelitis through repeated septic injections or by harboring septic vegetations on heart valves, in skin, or within veins that produce periodic septic emboli. Osteomyelitis caused by septic emboli in i.v.-drug abusers often demonstrates unusual organisms and a greater predominance of staphylococci from skin contamination; hence, culture results must be interpreted with care and a search for other foci of infection is mandatory for successful treatment.

Although the abovementioned mechanism usually is the main source for osteomyelitis of long bones in these patients, it cannot be seen as the most important factor in the development of acute and secondary chronic osteomyelitis of the jaws. More important factors in this patient group are the associated unhealthy lifestyle, like in patients suffering from chronic alcoholism, with malnutrition and self-negligence. A poor oral hygiene and the concomitant development of dental foci raise the risk for infection. An altered oral and skin flora, loss of mucosal barriers, and, in some cases, a behavioral indifference to disease and medical therapy also contribute to the higher incidence for infection in these patients. Besides an aggressive medical and surgical approach, nutritional support is advisable. Maintaining compliance in these patients for prolonged antibiotic therapy is a further challenge.

Patients with significant immunodeficiency, especially AIDS seems to develop a higher rate of acute and secondary chronic osteomyelitis of the jaws compared with a general healthy population. This has because of the impaired immune response, the clinical appearance of infections is generally different compared with the non-immuno-compromised host. Osteomyelitis of the jaws progresses faster with less clinical symptoms and is less responsive to conservative minimal invasive therapy approaches; therefore, the disease often transforms to a chronic stage. Cultures also frequently reveal unusual organisms in combination with more common oral pathogens (Marx 1991). The treatment of osteomyelitis of the jaws in AIDS patients should be addressed aggressive surgically and medically. Antibiotics should be culture oriented as soon as possible. Concomitant treatment of opportunistic infections and antiviral therapy must be coordinated closely with the infectious disease specialist.

8.3 Surgical Therapy

8.3.1 Acute and Secondary Chronic Osteomyelitis

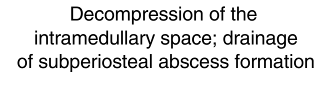
Surgery must be considered as the major pillar in the treatment of acute and secondary chronic osteomyelitis of the jaws. Surgical procedures in acute and secondary chronic osteomyelitis of the jaws pursue three major goals: (1) decompression of intramedullary pressure caused by the osteomyelitic process and drainage of subperiosteal abscess formation; (2) surgical debridement of infected tissue and removal of the infectious focus; and (3) bringing well-perfused tissue adjacent to the infected area. While local incision and drainage of abscess formation mainly facilitates decompression of intramedullary pressure, most other procedures mainly target surgical debridement, while decortication and (microvascular) reconstruction additionally bring well-perfused vital tissue to the affected area (Fig. 8.3).

8.3.1.1 Mechanisms of Surgical Treatment of Acute and Secondary Chronic Osteomyelitis of the Jaws

Local incision and abscess drainage, removal of loosened teeth, foreign bodies/implants, and sequestra, as well as local curettage and saucerization of the infected bone, can be considered as minor surgical procedures since they can usually be performed under local anesthesia and hence on an outpatient basis if desired. To the contrary decortication, resection, and (microvascular) reconstruction of osteomyelitic bone are clearly procedures performed under general anesthesia and in an inpatient setting. They are therefore considered as major surgical procedures.

In our own patient data considerable differences in the surgical therapy of acute and secondary chronic osteomyelitis were noted (Baltensperger 2003). While the percentage of patients with acute osteomyelitis treated conservatively was small and only little higher than patients with secondary chronic osteomyelitis, a substantially larger percentage of the latter group underwent major surgical procedures, mainly decortications (Table 8.4).

The most demanding decision for the surgeon is to determine the extent of the surgical debridement. Certainly removal of all necrotic soft and hard tissue as well as all granulation tissue must be achieved. Furthermore, tissue excision and bone curettage should be extended to tissue with sufficient perfusion, e.g., bleeding tissue (Marx 1991); hence, it is the extent of the lesion which dictates the extent of the surgery. One of the major goals of preoperative imaging is the assessment of the infected bone and soft tissue to accurately plan the surgical procedure. High-resolution CT scans are considered the gold standard in presurgical imaging since they determine most precisely the affected tissue which requires surgical removal. While conventional radiographs lag strongly behind the actual infectious process, especially in fast progressive osteomyelitis cases, MRI and radionuclide imaging studies, such as scintigraphy or PET,



Surgical debridement of infected tissue and removal of infectious focus

Bringing well-perfused tissue adjacent to the infected area

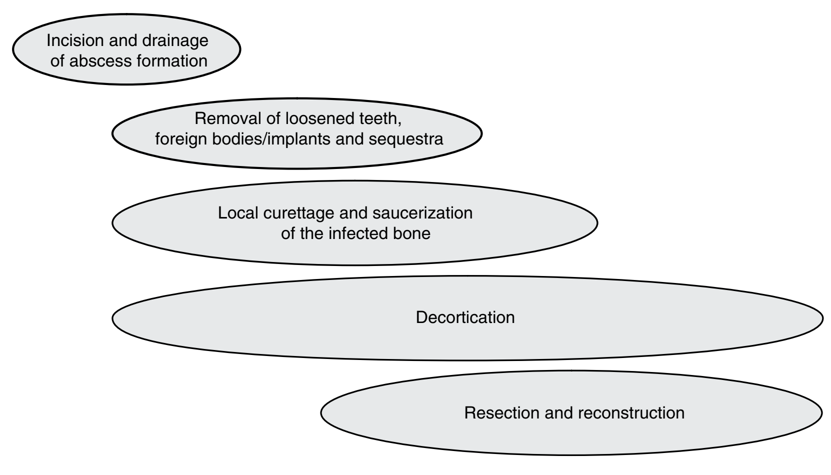


Fig. 8.3 Mechanisms of surgical treatment of acute and secondary chronic osteomyelitis of the jaws

tend to show a more extensive lesion which exceeds a necessary surgical debridement. Combined radionuclide and CT imaging studies, such as SPECT/CT and in recent years the up-and-coming PET/CT, may give a more accurate distribution of the extent of the osteomyelitis lesion; however, these imaging studies are not beneficial in the average acute or secondary chronic osteomyelitis case. In cases of primary chronic osteomyelitis or secondary chronic osteomyelitis with a predominant sclerosing character radionuclide imaging, on the other hand, may be advisable since determining the line between affected and nonaffected bone can be demanding.

Surgical debridement starts with removal of loosened teeth in the infected area, as well as removal of foreign bodies/implants and sequestra. In cases of more extensive infection, surgical procedures extend simultaneously. Local curettage, saucerization of the infected bone, decortication, and possibly resection followed by reconstruction may be necessary (Table 8.5).

The most typically performed procedures in acute and secondary chronic osteomyelitis are described below.

8.3.1.2 Sequestrectomy

Sequester formation is a classical sign of secondary chronic and advanced acute osteomyelitis cases. Usually a time frame of at least 2 weeks after onset of infection is necessary until presentation. In general, sequestra are confined to the cortical bone but may also be cancellous or cortical–cancellous. Once a sequester is fully formed, it may persist for several months in untreated cases before being resorbed or spontaneously expelled through the oral mucosa or the facial skin. Resorption of sequester is achieved by lytic activity of the osteoclast cells in the surrounding granulation tissue. Gradually the granulation tissue may ingrow the sequester and promote its degradation. If sequestra are not fully removed in treatment, partial, superficial healing may occur. Because sequester are avascular, they are poorly penetrated by antibiotics or HBO and hence are ideal breading grounds for bacteria. They serve as sources of exacerbations of the osteomyelitis when pus and granulation tissue accumulates around them. In rare cases of osteomyelitis of the jaws a sterile abscess formation around the sequester (Brodie's abscess), common to long bone osteomyelitis, occurs (Topazian 2002).

In untreated or insufficiently treated cases of secondary chronic osteomyelitis the body tries to isolate the sequester. A shell of bone produced by the periosteum, the so-called involucrum, serves as a barrier. This border may be perforated by tracts (cloacae) through which pus escapes to epithelial surfaces. Large sequester may influence the stability of the jaw and promote pathological fracture.

A more conservative approach to developing sequester formation is advocated by some authors in conjunction with supportive and antibiotic therapy. Once the sequester is formed completely, it may be removed with minimal surgical trauma. This minimally invasive procedure reduces subsequent bone and tooth loss (Topazian 2002). While this approach may be applicable in cases of localized osteomyelitis with superficial sequester formation, it is contraindicated in advanced cases with protracted spreading of the infection and sequester formation in more profound regions of the bone. Here a more aggressive surgical debridement is necessary which clearly must exceed the sole removal of sequester.

Table 8.4 Surgical therapy of acute and secondary chronic osteomyelitis of the jaws at the Department of Craniomaxillofacial Surgery Zurich 1970–2000 (From Baltensperger 2003)

	Acute osteomyelitis		Secondary chronic osteomyelitis		
	Cases		Cases		
	N°	%	N°	%	P-values
No surgical therapy	4	8.3	6	3.0	not significant
Surgical therapy	44	91.7	197	97.0	not significant
Major surgical procedures	32	66.7	174	85.7	0.002
Minor surgical procedures	29	60.4	115	56.7	not significant

In these advanced cases sequestrectomy is often the first part of the surgical debridement followed by decortication (see Fig. 8.8).

8.3.1.3 Saucerization

The next more extensive step in the surgical debridement of infected jawbone is saucerization. This surgical procedure describes the "unroofing" of the oral-faced jawbone to expose the medullary cavity for subsequent thorough debridement. The margins of necrotic bone overlying the focus of osteomyelitis are excised creating direct visualization of the infected medullary cavity. This allows direct access to formed and forming sequestra, granulation tissue, and affected bone. In a limited fashion the affected alveolar nerve may also be addressed; however, in cases of advanced acute and secondary chronic osteomyelitis with significant granulation tissue surrounding the inferior alveolar nerve, the created access by saucerization is insufficient.

The saucerization procedure is usually performed by an oral approach with the advantage of direct access to the jawbone and avoidance of facial scarring. The oral approach is, however, more challenging for collecting a noncontaminated specimen for microbiological investigation. Saucerization can be useful in early acute osteomyelitis cases and cases of limited extent. In early stages of the infection is benefits decompression of the medullary cavity and allow ready extrusion of pus, debris, granulation tissue, and avascular fragments.

This limited procedure minimizes morbidity for the patient and can usually be performed using local or general anesthesia on in an outpatient setting. Since the removal of bone by this procedure is limited, the strength of the mandible is not critically jeopardized and healing by secondary intention is sufficient. The lingual cortical bone rarely needs to be removed except where obviously necrotic bone or sharp crestal margins need to be addressed. The mylohyoid muscle attachments to the mandible provide a rich blood supply for the lingual bone and guarantee vascularization.

While the saucerization procedure is frequently used in mandibular osteomyelitis, it is rarely needed in the maxilla. Because of its thin cortex, sequestra usually form more rapidly and are exposed to the oral cavity, creating wider defects and possibly causing oroantral fistulas.

The saucerization procedure is described step by step in Table 8.6.

Table 8.5 Surgical management of acute and secondary chronic osteomyelitis. Depending on the extent of the infected bone, surgery has to be adapted, resulting in a smaller or larger procedure

	Incision and drainage of abscess formation
Extent of Surgery (– to +)	Removal of loosened teeth, foreign bodies/implants and sequestra
	Local curettage and saucerization of the infected bone
	Decortication
	Resection and reconstruction

8.3.1.4 Decortication

Decortication was first advocated for treatment of osteomyelitis of the mandible in 1917 and further described by Mowlem (1945). The application of this surgical procedure in conjunction with antibiotic therapy was later well described by Obwegeser (1960), Hjorting-Hansen (1970), and others. The decortication procedure quickly became an established and widespread procedure and must be seen as the workhorse in surgical osteomyelitis therapy.

In advanced acute and secondary chronic osteomyelitis of the jaws, especially the mandible, use of decortication promotes resolution based on the premise that the affected cortical bone is avascular and harbors microorganisms (Topazian 2002). The medullary cavity shows destruction and is largely replaced by granulation tissue and pus. Parenteral or per oral administered antibiotics cannot reach the affected region. Waiting for sequester formation and reducing surgery to sequestrectomy as described previously is not an option because of the advanced stage of the infection with risk for further spread, abscess formation, and cellulitis. Furthermore, the disadvantages associated with prolonged antibiotic therapy may become more prominent with time.

The major purpose of the decortication procedure is to remove the chronically infected cortex of the jawbone and gain access to affected medullary cavity to allow a sufficient decompression of intramedullary pressure and meticulous surgical debridement under direct visualization. Furthermore, this procedure allows bringing well-perfused tissue (e.g., masseter muscle) into contact with bone, promoting further healing.

While the decortication procedure was originally described as a procedure with an extraoral approach, the

Table 8.6 Saucerization of the mandible. (Step-by-step procedure modified after Topazian 2002)

Access to the bone by creating a mucoperosteal flap, usually using a gingival crest incision
Reflection of flap should be as limited as possible to preserve local bood supply
Affected teeth (loosened and other dental foci within the affected area) are extracted
The lateral cortex of the mandible is reduced using burs or rongeurs until the sufficient bleeding bone is encountered at all margins, approximately to the level of the unattached mucosa, thus producing a saucerlike defect
Local debridement is performed by removing granulation tissue and loose bone fragments from the bone bed using curettes
The debrided area is thoroughly irrigated with sterile saline solution with or without additional antibiotic such as Neomycin
If there is substantial local bleeding due to hyperemia caused by the inflammatory process, a medicated pack may be placed and serve as local compression device
The buccal flap is trimmed and a medicated pack (such as iodoform gauze lightly covered with antibiotic and local steroid ointment is placed for hemostasis and to maintain the flap in a retracted position. The pack is placed firmly without pressure and retained by several nonresorbable sutures, extending over the pack from the lingual to the buccal flap
The pack is remained in situ for several days up to 2 weeks or even more in some instances and may be replaced serveral times until the surface of the bed of granulation tissue is epithelialized and the margins have healed

standard approach is intraoral to prevent facial scarring. At the Department of Cranio-Maxillofacial Surgery in Zurich, which was founded by Hugo Obwegeser, the intraoral approach has been used whenever possible since the introduction of this procedure, following his third and fourth principles (Obwegeser 2001). This strict philosophy is reflected by our reviewed data of 173 decortication procedures performed on osteomyelitis cases from 1970 to 2000, which were all conducted by an intraoral access (Baltensperger 2003). The classical decortication procedure, as it is performed presently, at the Department of Cranio-Maxillofacial Surgery in Zurich is described and illustrated in Figs. 8.4–8.19.

8.3.1.5 Irrigation and Drainage

After completing surgical debridement of the osteomyelitic bone, the question of whether or not to place an irrigation drain must be decided. In the past decades some authors have advocated the use of drainage and/or irrigation devices (with/without) suction in analogy to the treatment of long bone osteomyelitis (Marx 1991; Topazian 2002). In advanced cases of acute and secondary chronic osteomyelitis, especially involving the mandible, the infection represents a deep-seated, well-established condition that may still retain necrotic tissue and microorganisms even after debridement. Irrigation drains and frequent irrigations reduce the number of microorganisms, the accumulation of toxins, and residual necrotic tissue (Marx 1991). Marx (1991) promotes as a general rule the use of debriding-type irrigants until the outflow has been clear for 24 h and then to switch to physiological irrigants such as normal saline or Ringer's lactate.

In our experience, drainage may be beneficial for 24–48 h to prevent hematoma formation. Postoperative closed-wound irrigation–suction shows little benefits once surgical debridement has been performed sufficiently. Furthermore, the administration is labor intensive and time-consuming and therefore requires a hospital setting, prolonging hospitalization.

8.3.1.6 Local Antibiotics

The use of systemic antibiotic treatment is well established in treatment of acute and secondary chronic osteomyelitis of the jaws and represents a major column in therapy (see Fig. 8.2). Besides the systemic administration of antibiotics, local application of antimicrobial drugs has become well established in the treatment of long bone osteomyelitis and also has gained some acceptance in osteomyelitis of the jaws.

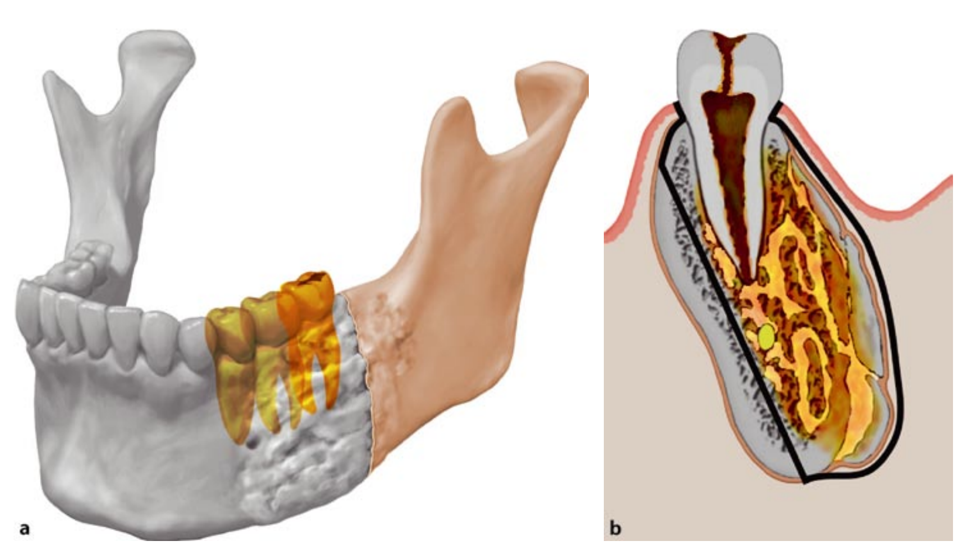


Fig. 8.4a,b Odontogenic secondary chronic osteomyelitis of the left mandible: The infection originated from the decayed lower left second molar and spread anteriorly to the second left premolar; posteriorly the affected bone reaches the ascending ramus (**a**). The coronal view demonstrates the decayed tooth and the amount of infected bone and periosteum that must be surgically removed in order to achieve a sufficient debridement (**b**)

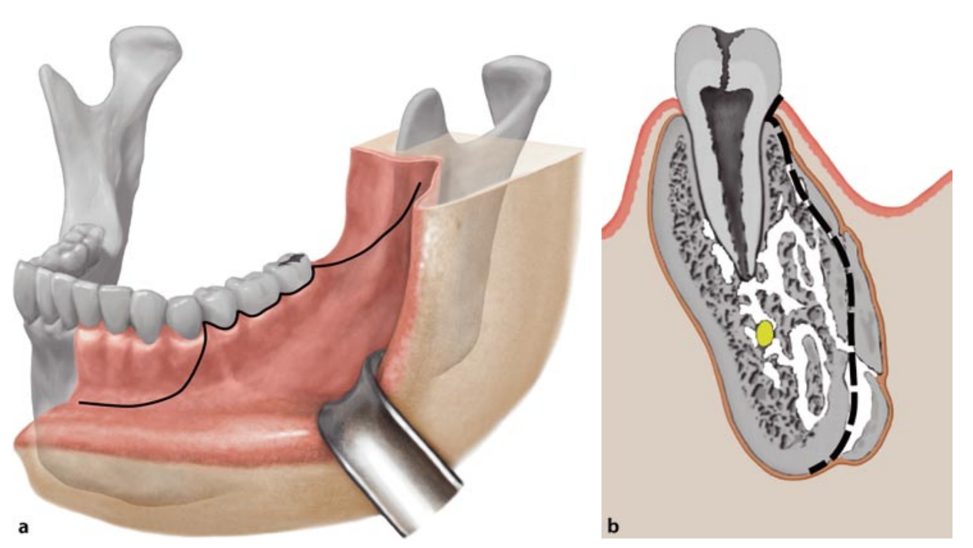


Fig. 8.5a,b Step 1: buccal incision along the gingival margin with vestibular extensions distally and mesially (**a**). Subperiosteal dissection creating a full-thickness mucoperiosteal flap to expose the affected bone (*dashed curve*, **b**). Note that the subperiosteal newly formed bone may not easily be separated from the affected periosteum

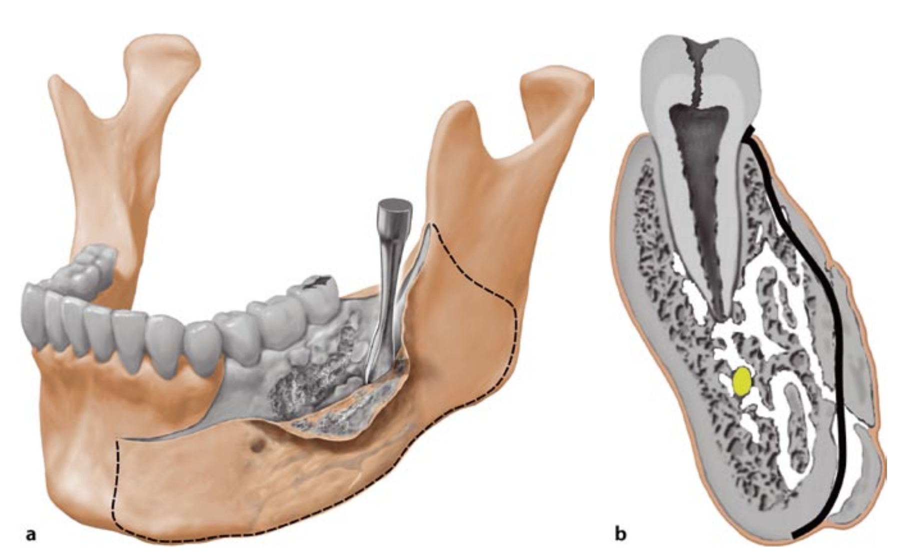


Fig. 8.6a,b Subperiosteal dissection and exposure of the affected region (**a**). Coronal view (**b**)

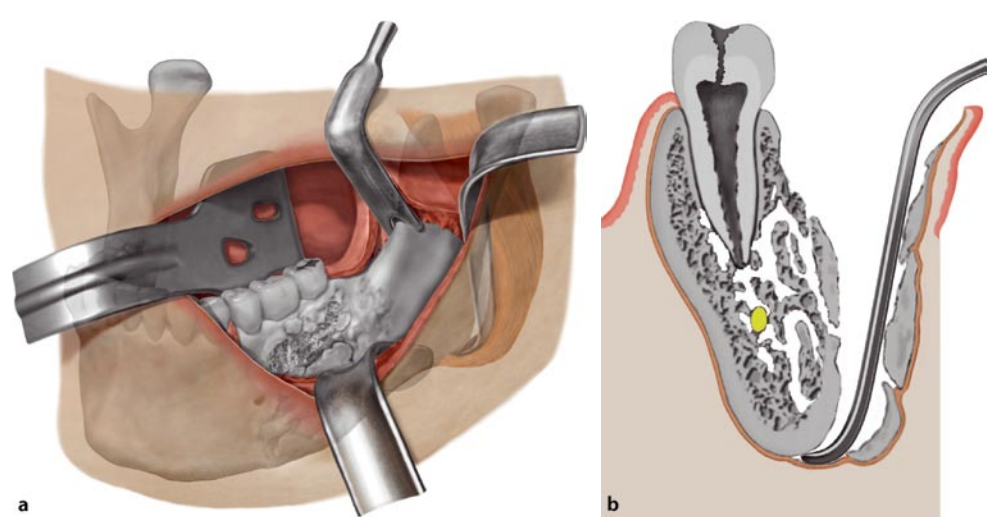


Fig. 8.7a,b Subperiosteal dissection and exposure of the affected region (**a**). Insertion of a retractor subperiosteally at the inferior border of the mandible to facilitate exposure of the affected mandibular corpus (**b**)

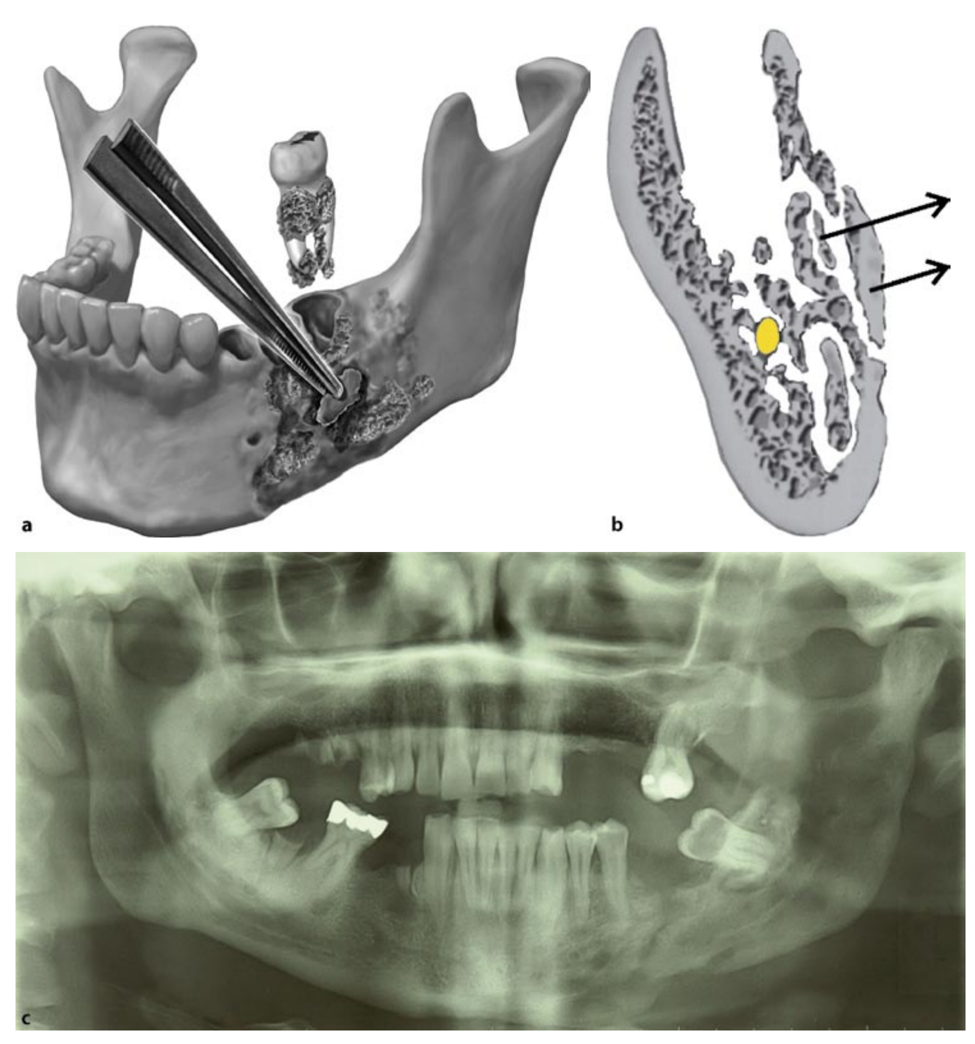
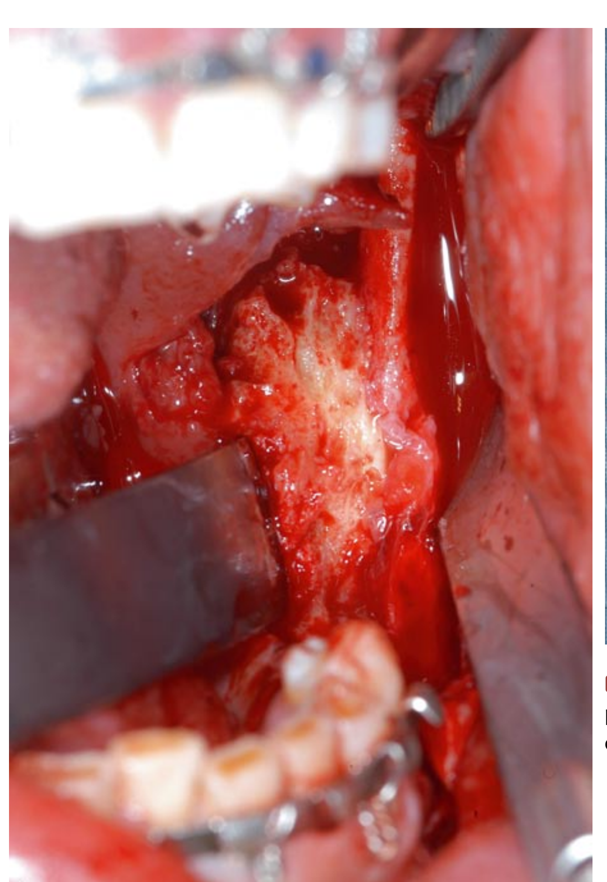


Fig. 8.8a–e Removal of the odontogenic focus and the teeth in the affected region and removal of sequester (**a,b**). Patient with extensive secondary chronic osteomyelitis of the left mandible with formation of a large sequester at the base of the mandible in the premolar region and a pathological fracture: orthopantomography at initial presentation (**c**). **d,e** *see next page*. (Courtesy of N. Hardt)



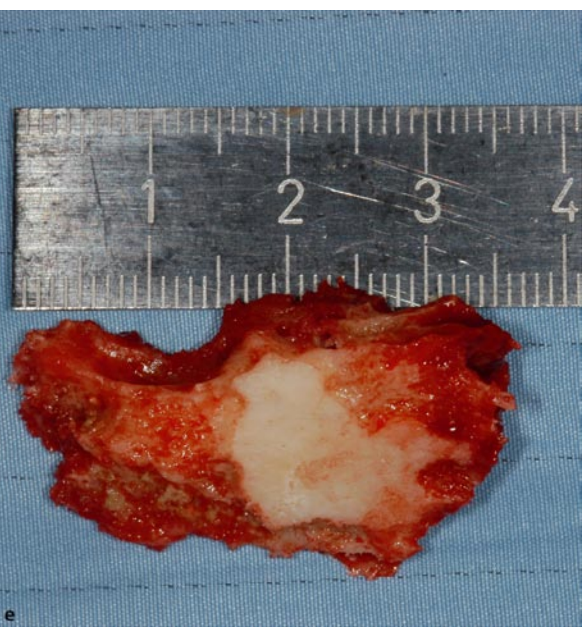


Fig. 8.8a–e (*continued*) Intraoperative view of the same patient demonstrates the large sequester (**d**). The large sequester after surgical removal (**e**). (Courtesy of N. Hardt)

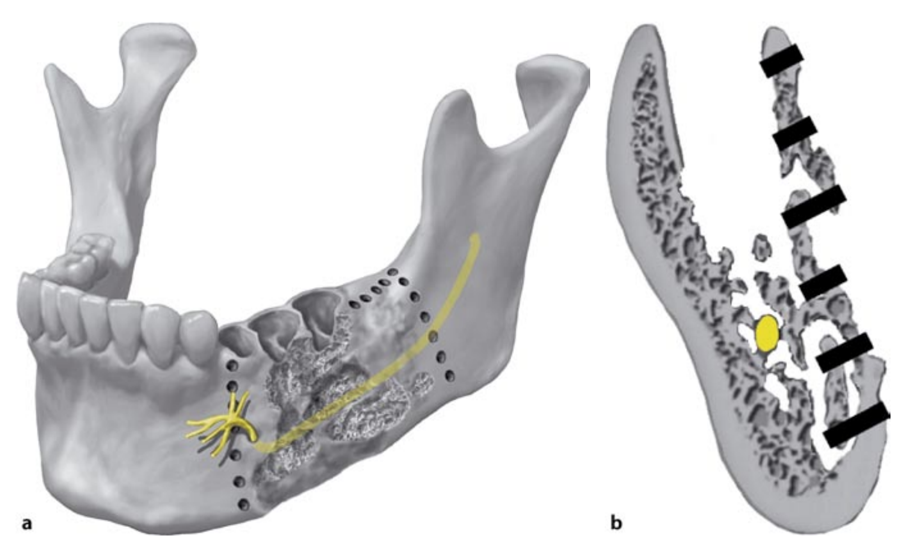


Fig. 8.9a,b The margins of the intended area of decortication are marked with a burr. Note that the distal and mesial boarders are selected in an area where well-vascularized and healthy bone are assumed, usually 1–2 cm beyond the affected area (**a**). The coronal section demonstrates that the area of decortication should be extended caudally according to the extension of the affected bone, including the inferior boarder of the mandible, if necessary (**b**)

Fig. 8.10a,b After demarcation of the intended area of decortication as described in Fig. 8.9a, a long Lindemann burr is used to perform multiple monocortical decortication osteotomies on the buccal cortex of the mandible leaving a distance of approximately 1 cm between the decortication osteotomies (**a**). When performing the osteotomies it should be stressed that they are strictly limited to the buccal cortex of the mandible to avoid damage to the inferior alveolar nerve (**b**)

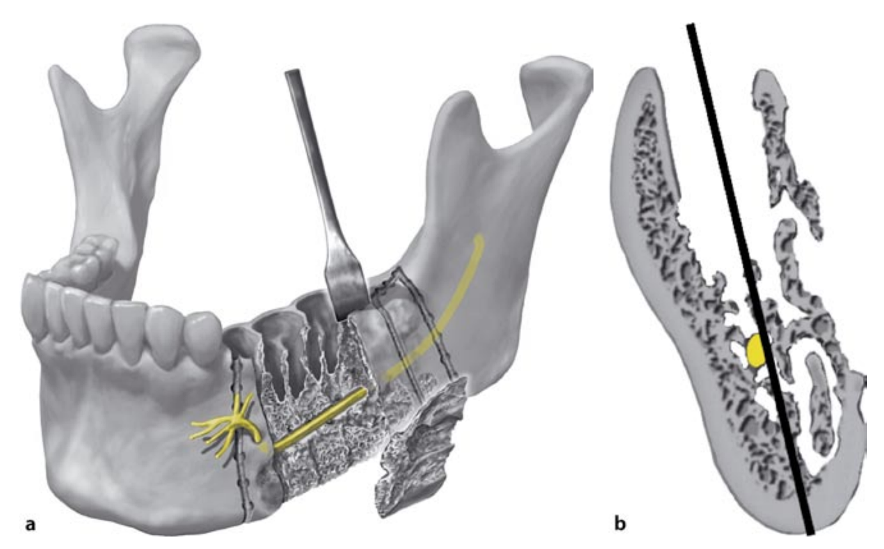


Fig. 8.11a,b The buccal cortical bone and the inferior border are then removed with a chisel, lane by lane, until bleeding bone is encountered. If necessary, additional osteotomies and removal of buccal cortical bone may be performed. The extent of the decortication is dictated by the amount affected bone, which is poorly vascularized with necrotic compartments

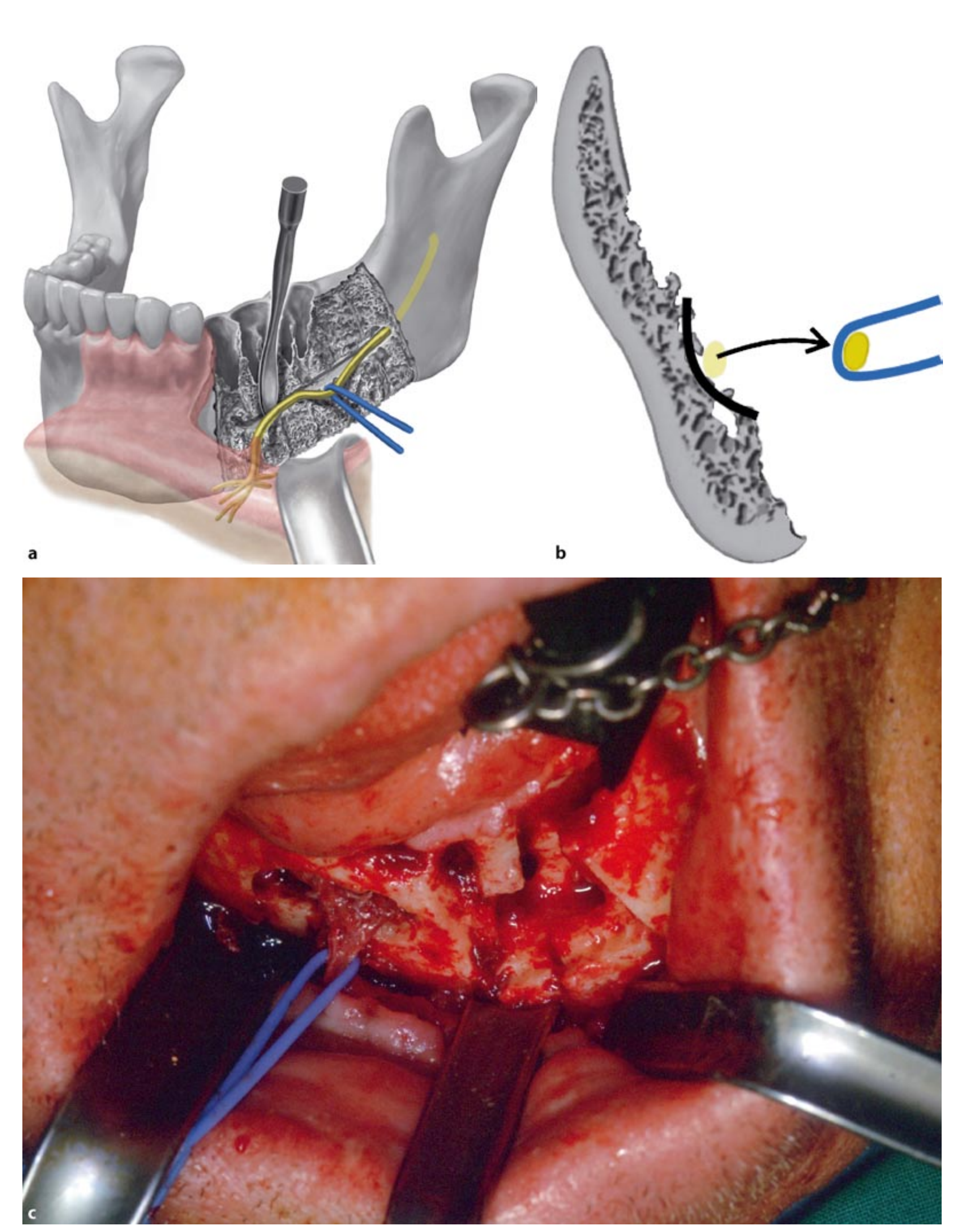


Fig. 8.12a–c Mobilization (neurolysis) of the interior alveolar nerve is performed to allow access to the surrounding deeper areas of affected bone. The nerve may be marked with a vessel loop. **c** An intraoperative view of this step of the decortication: The decortication has started mesially in the unaffected part of the anterior mandible. While the decortication advances distally to the posterior part of the mandibular body, the inferior alveolar nerve is liberated and mobilized (lateralization) after separating it from the incisive branch, hence allowing further surgical debridement (case report 7, Chap. 12)

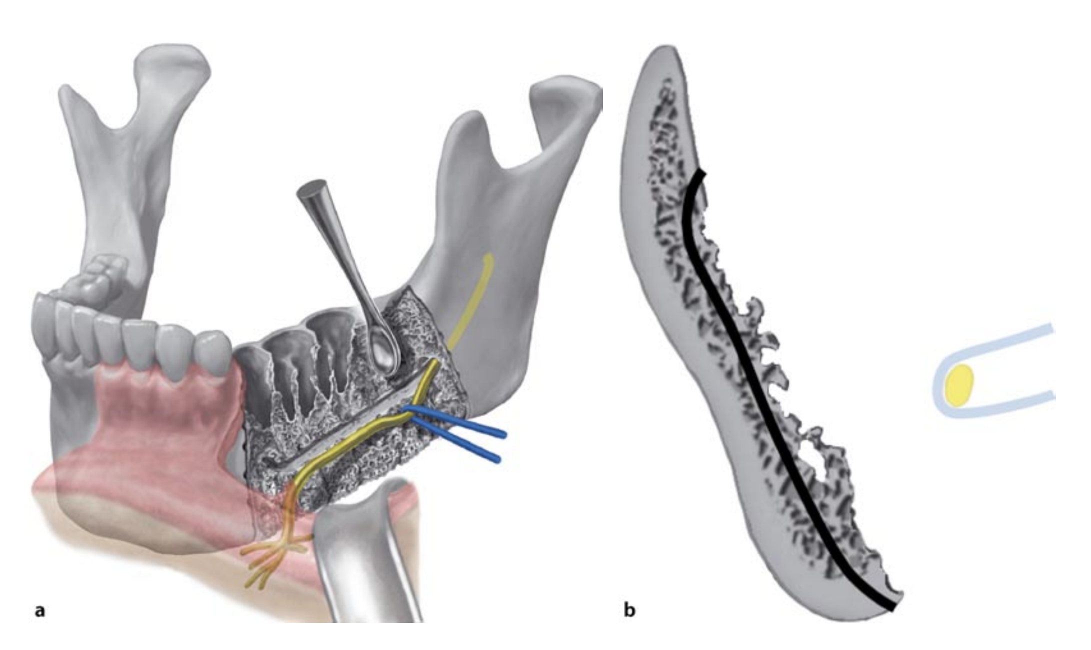


Fig. 8.13a,b Meticulous removal of affected bone and granulation tissue is performed (**a**). The curettage is completed when vital bone (e.g. well-vascularized bleeding bone) is visible. In certain instances it may be necessary to remove all of the spongiosa bone tissue until the lingual cortex is reached (**b**)

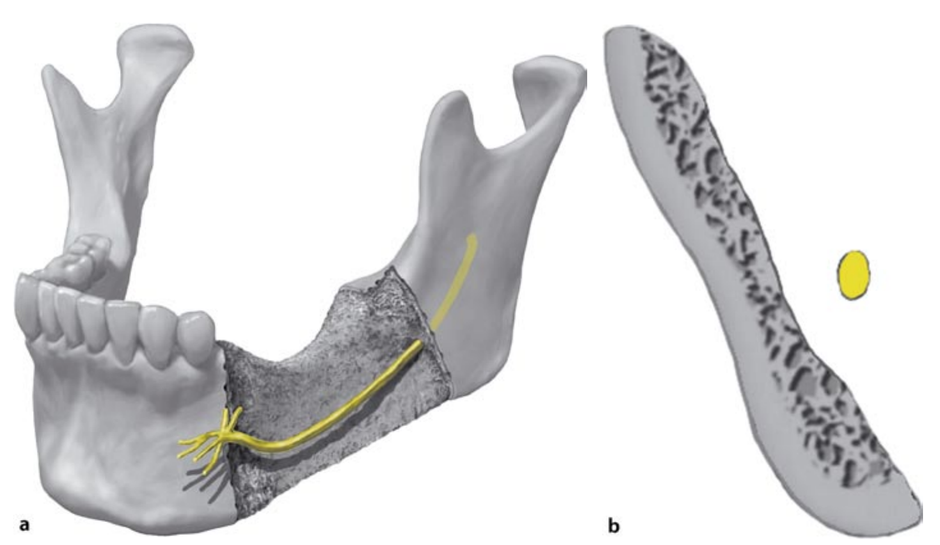


Fig. 8.14a–e Mandible after completed decortication and surgical debridement. The remaining bone represents the remaining vital bone tissue (**a,b**). **c-e** *see next page*



Fig. 8.14c–e (*continued*) Mandible after completed decortication and surgical debridement.The status after surgical decortication of the right mandibular corpus with partial neurolysis of the inferior alveolar nerve (**c–e**; case report 4, Chap. 12)



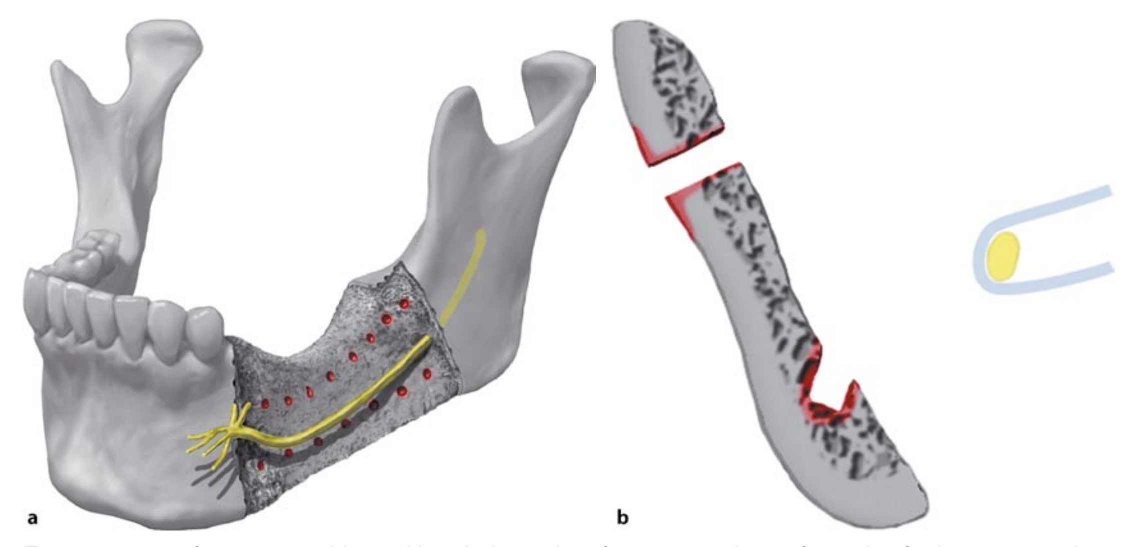


Fig. 8.15a–c If necessary, additional burr holes and perforations can be performed to facilitate contact better in vascularized deeper bone compartments or to the lingual periosteum (**a,b**). **c** *see next page*

Fig. 8.15a–c (*continued*) An intraoperative view after surgical debridement (decortication) of the anterior mandible and perforations of the lingual cortical bone (**c**). The mental/inferior alveolar nerve has been mobilized to allow sufficient debridement (case report 11, Chap. 12)

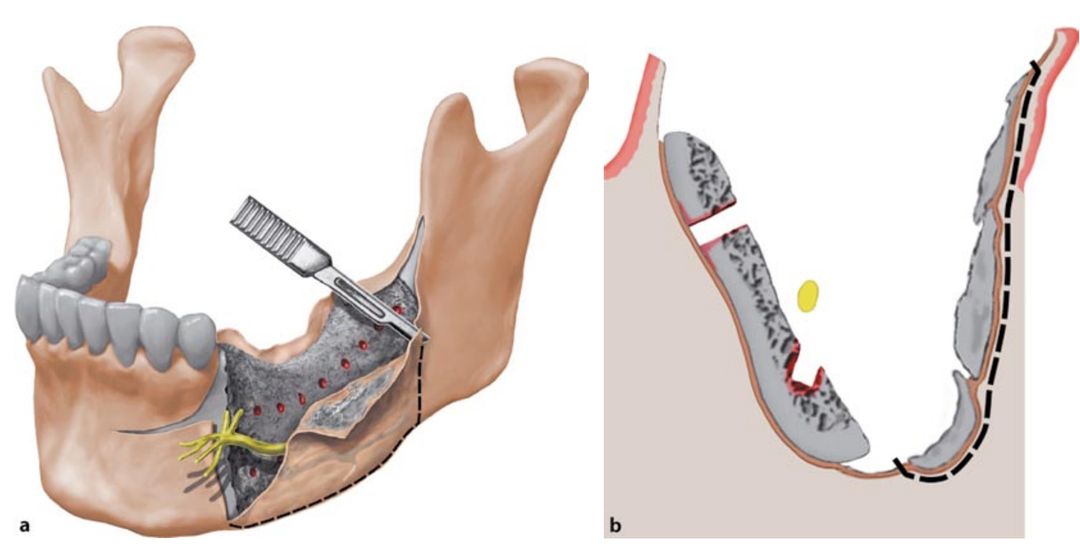


Fig. 8.16a,b Resection of affected buccal periosteum with areas of neoosteogenesis

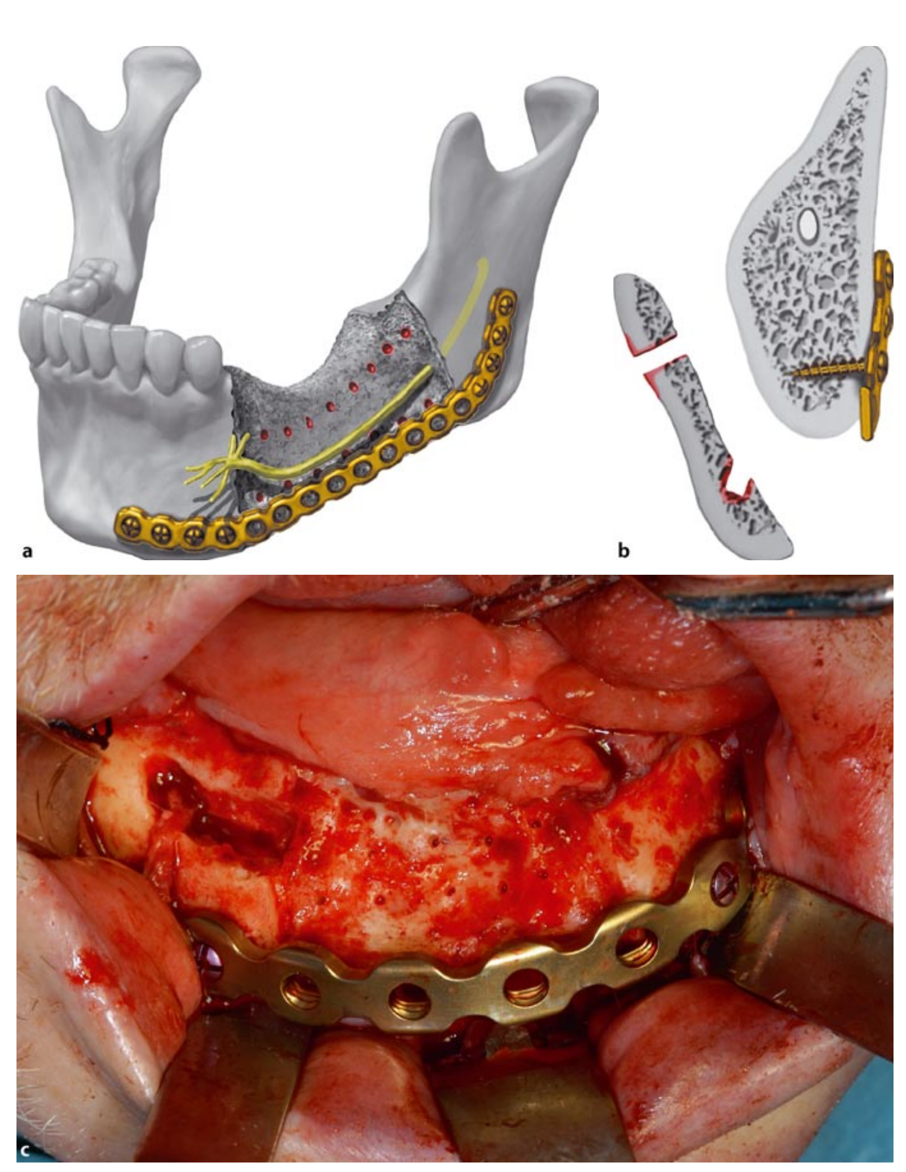


Fig. 8.17a–c If extensive debridement was required and the remaining bone is suspected to be prone to fracture, appropriate stabilization and reconstruction should be performed. In this case stabilization of the left mandible was achieved by osteosynthesis with a thick reconstruction plate. The surgical site after completed decortication and stabilization of the anterior mandible with reconstruction plate is shown in **c** (case report 11, Chap. 12)

Fig. 8.18a,b Primary closure is achieved to ensure close contact of the bone bed to the well-vascularized soft tissue. Irrigation tubes and/or antibiotic beads are usually not placed

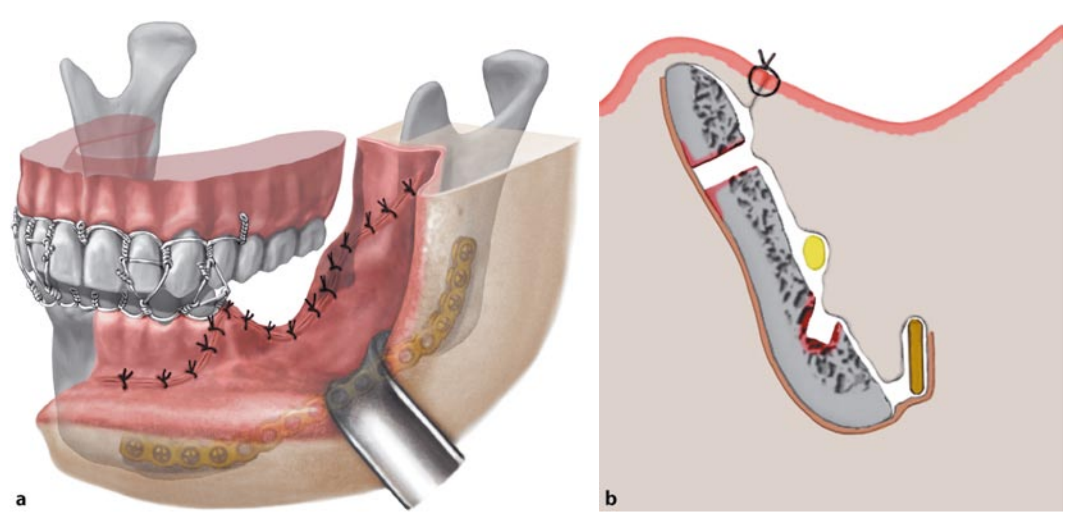


Fig. 8.19a–c Maxillary–mandibular fixation may be performed if additional stabilization and immobilization is required. Postoperative orthopantomography of a patient with extensive secondary chronic osteomyelitis of the left mandible after surgical decortication is shown in **c** (case report 6, Chap. 12): the maxillary–mandibular fixation for 6 weeks with wire stents was additionally performed for sufficient stabilization and immobilization of the operated left mandible to ensure healing without complication **c** *see next page*

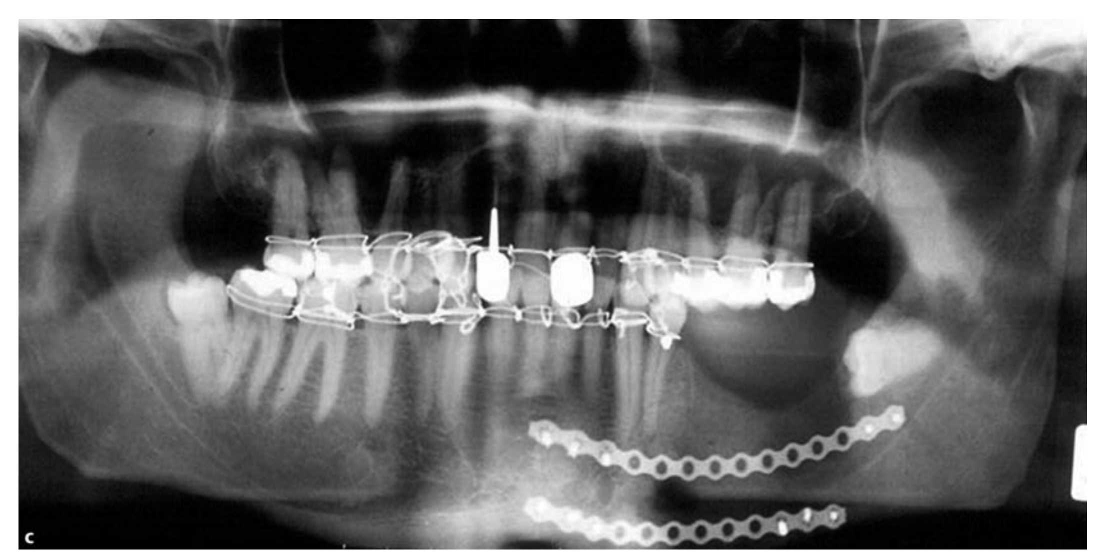


Fig. 8.19a–c (*continued*) Maxillary–mandibular fixation may be performed if additional stabilization and immobilization is required. Postoperative orthopantomography of a patient with extensive secondary chronic osteomyelitis of the left mandible after surgical decortication is shown in **c** (case report 6, Chap. 12): the maxillary–mandibular fixation for 6 weeks with wire stents was additionally performed for sufficient stabilization and immobilization of the operated left mandible to ensure healing without complication

Local antibiotics can be administered by continuous local infusion, irrigation, and suction, or in the form of antibiotic-impregnated acrylic beads. While the former application is labor intensive and time-consuming, with high demands to the nursing and medical staff, the latter is usually administered after surgical debridement prior to closure of the wound. Antibiotic-impregnated acrylic beads are used to deliver high concentrations of antibiotics into the wound bed and in the immediate proximity to the infected bone (Fig. 8.20; Alpert et al. 1989; Chisholm et al. 1993; Grime et al. 1990; Härle and Ewers 1984).

The antibiotic drug (usually tobramycin or gentamycin) is gradually released from nonresorbable polymethylmethacrylate (PMMA) beads, which are removed in a second procedure through a small skin or mucosa incision. (Degradable carriers for the antibiotic drug are currently being investigated to replace PMMA and hence avoid a second procedure for removal.) The local antibiotic release produces high local concentrations but only low systemic concentrations, thus reducing the risk of toxicity.

In general, the use of local antibiotics is not indicated for the standard case of acute and secondary chronic osteomyelitis of the jaws. A thorough local debridement, followed by a prolonged antibiotic therapy, is usually sufficient.

In cases of extensive secondary chronic osteomyelitis of the jaw with large destruction of the mandible, when a continuity defect results after debridement which needs bridging with a reconstruction plate, some authors advocate the additional benefits of placing a string of antibiotic-impregnated beads at the surgical site against the bone. The beads are then subsequently removed in a second procedure prior to final reconstruction (Chisholm et al. 1993). In our patient data (Baltensperger 2003) local antibiotics were only used in few cases of secondary chronic osteomyelitis with a complicated course where eradication of the infection was not achieved after the first major surgical debridement.

8.3.1.7 Immobilization and Fracture Treatment

Immobilization and stabilization of the surgical site are an integral part in the surgical therapy of advanced acute and secondary chronic osteomyelitis of the jaws, e.g., the mandible. Immobilization reduces the number of microorganisms by eliminating the pumping action of jaw motion, which allows a continuous influx of bacteria into the surgical wound. Immobilization of the



Fig. 8.20 Orthopantomography of a patient with secondary chronic osteomyelitis of the right mandible after surgical decortication: A string of nonresorbable polymethylmethacrylate (PMMA) beads, which carries gentamycin, was placed at the surgical site after decortication. The PMMA beads are connected to each other with a radiopaque string for better visibility on postoperative imaging, facilitating localization for secondary surgical removal (Courtesy of N. Hardt)

mandible further promotes tissue perfusion and hence oxygenation with all its benefits by facilitating capillary ingrowth. The constant shearing forces produced by jaw movements may disrupt new ingrowing capillaries, leading to hypoxic wounds and additional scar tissues (Marx 1991).

If an infected fracture is the source of osteomyelitis or surgical debridement of the osteomyelitic bone results close to or in a continuity break of the mandible, adequate stabilization must be performed after sufficient debriding is assured. This may require usage of a strong plate such as a reconstruction plate (Fig. 8.17a,b). Despite the microorganism-harboring ability of reconstruction plates, only these plates guarantee sufficient strength to ensure immobilization of the surgical area. An alternative would be the use of an external fixation device and a second-stage reconstruction when the infection subsides. This approach, however, requires an additional procedure. Further drawbacks of this treatment protocol are the impractical handling for the patient, which often prolong hospitalization and facial scarring associated with an external skeletal pin fixation.

In our experience, the use of internal reconstruction plates, if necessary, has been proven to be a safe and predictable procedure with a good outcome. A meticulously performed surgical debridement and a prolonged antibiotic therapy after surgery are necessary to guarantee success of this protocol.

In some instances, maxillomandibular fixation (MMF) may help to immobilize the affected region and hence facilitate healing (Fig. 8.19a).

8.3.1.8 Resection and Reconstruction

The question as to whether reconstruction of a defect after surgical debridement should be addressed simultaneously or in a second-stage procedure is addressed differently in the literature. Marx (1991) advocates a two-stage procedure to reconstruct continuity defects resulting from surgical debridement of osteomyelitis with reconstruction of the bone commencing as early as 3 months after debridement, provided that skin and mucosa are intact and the tissue is free of contamination and infection.

The two-stage procedure obviates simultaneous reconstruction and thus placement of a reconstruction plate and/or an immediate bone graft, which possible harbors the risk of contamination and infection.

Obwegeser (1966, 1978) and Sailer (1976, 1984) successfully demonstrated in a series of patients that si-

multaneous reconstruction after surgical debridement of acute and secondary chronic osteomyelitis cases involving the jaw could be successful provided that a meticulous debridement and subsequent antibiotic therapy were implemented.

In general, a two-stage procedure is always safer than a simultaneous reconstruction using a bone graft; however, regardless of the preferred protocol, a meticulous debridement is always the prerequisite for successful treatment of advanced acute and secondary chronic osteomyelitis cases.

While smaller bone defects may be filled with free autologous bone, larger defects are preferably addressed using microvascular bone (and soft tissue) grafts. Smaller bone defects can usually be addressed through an oral approach; larger reconstruction, especially when microvascular techniques are involved, require a larger, extraoral approach.

In cases of a generalized bone pathology affecting all bones, such as osteopetrosis or bisphosphonate therapy, reconstruction of surgical defects resulting from debridement with bone grafts is difficult, if not impossible, because all donor sites are affected with the same pathology.

8.3.1.9 Other Therapy Modalities

Compromise of local vascularization by (septic) thrombosis with impairment of bone blood supply and subsequent development of necrosis is a major pathophysiological mechanism in the development of acute and subsequent secondary chronic osteomyelitis of the jaws, especially the mandible. This in mind, it is only logical that therapeutic strategies aim to improve vascularization and prevent as well as resolve developed thrombosis.

Bartkowski et al. (1994) treated a series of 52 patients with acute or secondary chronic osteomyelitis, including 38 patients in whom the mandible was affected. They used moderate bone surgery in 21 patients, while the group of 52 patients was excluded from surgery aside from biopsy procedures. The majority of cases received a combined treatment of antibiotics and heparin (A+H), and an additional, smaller group with advanced secondary chronic osteomyelitis streptokinase was used additional to antibiotics and heparin (A+H+S). As a conclusion of this study, this new approach was shown to be effective especially in complicated and advanced cases; however, their long-term results are not significantly different to results in conventional treatment of acute and secondary chronic osteomyelitis of the jaws using surgery and antibiotics. Furthermore, especially the use of systemic streptokinase harbors a significant risk for complications which limits its use or possibly outweighs the benefits.

8.3.2 Primary Chronic Osteomyelitis

Because primary chronic osteomyelitis responds to treatment inconsistently (Vargas et al. 1982), all treatment options should be considered and applied on an individual basis. As described previously, the course of early onset of primary chronic osteomyelitis (juvenile chronic osteomyelitis) may differ from the adult type. In addition, the stage of disease may be different in an earlier period compared with a later stage. In the decision-making process, the frequency of onset with pain, swelling, and limitation of mouth opening should be taken in to account as well; therefore, extent and aggressiveness of treatment may also differ. The large volume and extent of affected bone in most cases may suggest that complete surgical removal would be the best option.

Montonen et al. (1993) described in a series of 41 cases of diffuse sclerosing osteomyelitis the effect of the decortication procedure (described previously in this chapter). The reported data refer mostly to patients with adult-onset primary chronic osteomyelitis of the jaw. Symptoms recurred in 75% of the cases within 12 months after surgery in their patient group; however, the authors observed that patients who exhibited improvement were significantly older and more often edentulous than patients in whom the symptoms recurred. Because involvement of reconstructed bone is frequently observed, resection and second-stage reconstruction should be considered carefully in late stage of disease (Eyrich et al. 1999).

Especially in the early-onset cases of disease we do not favor full-thickness resection of bone such as continuity resection or hemimandiblectomy since some of the juvenile patients have shown remission at the end of bony growth. Those patients may still show the typical sclerotic bone pattern for some time; hence, clinically the disease may transform into a more silent stage of disease with no need for therapeutic intervention. In addition, extensive resection may not guarantee control of disease and such aggressive interventions may even cause functional loss and result in affection of transplanted bone.

In our experience results of neither early-onset (juvenile) nor late-onset (adult) cases treated with large resections of bone and reconstruction of bone with either rib or even free microvascular grafts were not always

promising; however, because of adverse experiences in our institution early on, we were not able to compare a large number of resected and transplanted cases to cases where no resection was performed.

Especially in the early stage of disease, operative procedures, such as localized removal of all necrotic tissue and decortication, are usually successful (Eyrich et al. 1999). In an early stage of the disease with a large volume of altered bone and a high frequency of active periods, decortication corrects bone deformity, removes necrotic tissue, improves bony blood perfusion, and in most cases leads to a decrease in frequency of onset.

Interestingly, in our series of patients with primary chronic osteomyelitis we have never come across a single case where the disease resulted in a pathological fracture such as in secondary chronic osteomyelitis needing resection and reconstruction. Obviously the affected bone still has enough elasticity not to fracture and even has shown sufficient regenerative potential to perform orthognathic surgery (case report 16, Chap. 12)

In patients with multiple unsuccessful interventions and elderly medically compromised patients conservative therapy plays an important role. Conservative therapy involves HBO, nonsteroidal antiinflammatory drugs (NSAIDS), antibiotics, steroids, as well as bisphosphonates and other drugs.

Concerning HBO, data are contradictory and the overall role of HBO remains unclear. If HBO (twice daily sessions at 1.4 atmospheres for 45 min cycles) is applied, it seems to be important that the treatment period consist of a minimum of 20 or more sessions and that antibiotics be administered along with the HBO treatment.

Patients respond to administration of NSAIDs with clearly reduced symptoms; however, during the course of disease NSAIDs may loose some effectiveness. In a long-standing therapy with NSAIDs side effects, such as gastro-intestinal and kidney problems, must be taken in to account.

The NSAID and steroids block the inflammatory cascade on different mediatory levels. In long-standing refractory cases of diffuse osteomyelitis steroids may be considered, especially if NSAIDs are ineffective. In our experience a single dosage of 50 mg prednisone leads within 12 h to immediate and mostly to complete relief of pain and swelling (Eyrich et al. 1999).

Patients treated with long-term antibiotic medication showed no, or at least a decreased, frequency of mild symptoms while on medication. Interestingly, symptoms usually reoccur within 2 weeks after the last dosage of antibiotics is given. The spectra of effective antibiotics are predominantly those targeting anaerobes, including clindamycine, amoxicillin, metranidazole, and tertracyclines.

Recently, several case reports reported favorable responses to pamidronate and other bisphosphonates (Compyerot-Lacassagne et al. 2007; Sugata et al. 2003; Yamazaki et al. 2007; Soubrier et al. 2001). Montonen et al. (2001) published a series of ten patients with diffuse sclerosing osteomyelitis which were treated on a double-blind basis with i.v. disodium clodronate. The appliance of the bisphosphonate did not result in better immediate pain relief than placebo administration; however, 6 months after treatment, there was a statistically significant difference in pain intensity between the groups, with the disodium clodronate group experiencing significantly less pain.

Although the effects of bisphosphonates on bone are still readily discussed, some mechanisms have recently become evident. Both bone-specific alkyne phosphatase (bone formation marker) and pyridinoline cross-linked carboxyterminal telopeptide of type-I collagen (bone resorption marker) showed a marked decrease with pamidronate. It may therefore be useful in the treatment of primary chronic osteomyelitis due to its inhibitory effect on bone turnover (Yamazaki et al. 2007).

We also have observed good response to intravenous Pamedoarte therapy in our patients (case report 13, Chap. 12). In our opinion, this therapy, however, should be reserved to patients who not respond to NSAIDs or steroids. Mild reactions to Pamidronate therapy, such as low-grade fever and lassitude, is well known, and thus far severe adverse reactions in patients with chronic diffuse osteomyelitis have not been observed. Effects such as bisphosphonate-induced osteochemonecrosis of the jaws, as seen under long-term therapy, do not usually appear since drug administration in patients with primary chronic osteomyelitis is only recommended in association with periods of onset and is therefore only used for a short period; however, because of its unknown teratogenic potential, therapy in young patients should be carefully considered. Overall, Pamidronate seems to be an effective second-line therapy (Compyerot-Lacassagne et al. 2007).

In cases of syndrome-associated primary chronic osteomyelitis treatment includes NSAIDS at sufficient dosage levels and, in refractory cases, administration of sufusalazine. Few persistent cases may require administration of methotrexate (Eyrich 1999).

In summary, it must always be kept in mind that the main goal, especially in patients with primary chronic

osteomyelitis, must be to eliminate or at least ameliorate clinical symptoms, since a cure cannot be guaranteed in this still poorly understood disease. In our experience, the chief principle *primun ne nocere* should be applied vigorously in primary chronic osteomyelitis before administering aggressive (surgical) therapy, especially when dealing with young patients. Even though the disease may not yet be curable, change of course and severity should be considered a sign of success.

8.4 Follow-up and Outcome

8.4.1 Acute and Secondary Chronic Osteomyelitis

8.4.1.1 Follow-up

Termination of treatment and definition of the follow-up period is a pivotal and difficult decision in the management of acute and secondary chronic osteomyelitis. It is in the nature of this disease that recurrence may appear after a long period where the patient may be free of symptoms. Reactivation of occult and/or residual bone infection may result if the balance of aggressor and host defense systems is crucially disturbed (see Fig. 2.5, Chap. 2). Recurrence of secondary chronic osteomyelitis has been reported in the literature as late as 49 years in long bones (Widmer et al. 1988). In our own patient data a case of secondary chronic osteomyelitis of the mandible with reactivation 10 years after termination of treatment was identified (Baltensperger 2003).

In clinical practice such long-term follow-up for every osteomyelitis patient is costly and unnecessary, if not impossible.

The end point of therapy should first be decided based on clinical judgment. Cessation of suppuration, closure of wound or development of granulation tissue, and a reduction or complete remission of clinical signs should be attained. Conventional radiographs (e.g., orthopantomograms) can be used as follow-up imaging studies; however, their limitations in sensitivity must be taken into account and, in cases with a complicated course, CT scans are preferable. Signs of remission in follow-up imaging studies are the lack of further osteolysis, sequestration, and periosteal reaction (neoosteogenesis). Ideally, follow-up images taken 6–12 weeks after surgery will show some form of early remodelling (Fig. 8.21). Another method for monitoring the course of acute and secondary chronic osteomyelitis are bone scans; however, to achieve maximal significance several bone scans should be compared and ideally a bone scan prior to start of treatment is obtained for baseline. Furthermore, it must be taken in account that in postoperative scans the activity is increased. This is explained by intensive remodelling process and repair mechanisms which are to be interpreted as a physiological response of the bone. In analogy to fracture healing a postoperative bone scan remains positive for several weeks and should not be misinterpreted as a relapse of infection. Usually it takes 2–4 months for uptake values of radioactive tracer to slowly decrease and turn to normal levels, providing complete cure.

In our patient data (Baltensperger 2003) the mean follow-up period of cases of acute and secondary chronic osteomyelitis was approximately 1 year; however, the follow-up period in the vast majority of acute osteomyelitis cases was 3–6 months, and in patients with secondary chronic osteomyelitis it was approximately 9–12 months for the average case.

8.4.1.2 Outcome

The outcome of cases of acute and secondary chronic osteomyelitis is only documented scarcely in the literature. In a recent survey by Kim and Jang (2001) in 49 patients with secondary chronic osteomyelitis of the jaws who were treated with surgery followed by 2 weeks of intravenous antibiotics, followed by 6 weeks of oral antibiotics, they achieved a successful outcome in 94.9% of patients compared with only 60% of control patients who received surgical therapy alone. In our own patient data, which overlooks patients treated over a time period of 30 years, despite some differences in the type and duration of the antibiotic therapy and the occasional use of adjunctive HBO, the treatment of acute and secondary chronic osteomyelitis of the jaws consisted, with few exceptions, of the aforementioned main columns of osteomyelitis therapy: surgery and (prolonged) antibiotics. In 72% of the treated patients with acute and secondary chronic osteomyelitis the patient was free of symptoms at the end of the follow-up period. In 20% of the treated patients residual symptoms such as mild pain/local discomfort and/or hypoesthesia were noted. Closer inspection of this patient group, however, revealed that theses symptoms were almost always related to postsurgical effects rather than persistent infection. Scar formation after surgery and residual nerve damage due to surgical debridement are seen as probable causes for these observations. Not surprisingly, therefore, hypoesthesia



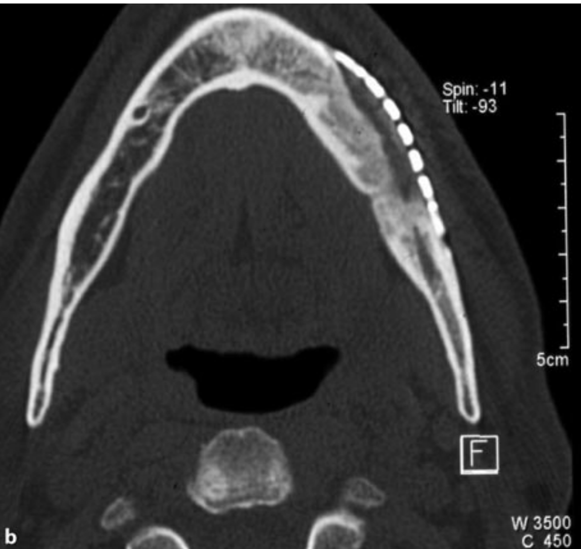


Fig. 8.21a,b Postoperative CT scans after an extensive surgical debridement (decortication) in a case of secondary chronic osteomyelitis of the left mandible (**a**) and follow-up CT scans after 6 months: note the significant bone remodeling which has taken place (**b**). (This case is described in detail in Chap. 12, case report 6)

was most prominent in patients who received extensive decortication of the mandible with neurolysis of the inferior alveolar nerve.

In the remaining patients the infection was still present to some degree at the end of the follow-up period and patient follow-up was incomplete due to various reasons. A careful review of this patient group showed that either the infection was not treated aggressively enough in the beginning and therefore was prolonged, or the patient lacked compliance to treatment.

8.4.2 Primary Chronic Osteomyelitis: Follow-up and Outcome

Since the course of primary chronic osteomyelitis cases is unpredictable, a long-term follow-up for several years usually is advisable. Especially cases of early-onset primary chronic osteomyelitis, in our experience, tend to show an amelioration or even cessation of symptoms after termination of skeletal growth. Observing the patient during puberty and adolescence is therefore paramount to understand possible effects of administered therapy and the spontaneous course of the disease.

Signs of remission are primarily judged on a clinical basis. In our patient series the decrease of frequency and intensity of active episodes of the disease are considered to be clinical remission. While soft tissue swelling usually disappears with the declining active episode, bony deformities due to primary chronic osteomyelitis may persist (Fig. 8.22a–d) or a (partial) return to normal contours may be observed (Fig. 8.23a–f).

The radiological appearance of late-stage or even inactive primary chronic osteomyelitis often demonstrates a strong residual sclerosis with a small number, or absence, of osteolysis and marked periosteal reaction (Figs. 8.22e,f, 8.23a–f).

In our experience, persisting osteolysis in the absence of clinical symptoms must not be interpreted as active regions which require therapeutic (surgical) intervention; however, we do recommend to carefully follow-up these patients. In some instances teeth in the affected area may persist, reacting negatively to vitality testing (e.g., with co2-Ice) even after a long period in which no further symptoms are clinically apparent; however, this must not lead to the wrong assumption that these teeth are nonvital and lack pulpal perfusion, and endodontic treatment must be avoided in the absence of further clinical and radiological evidence of root canal degeneration.



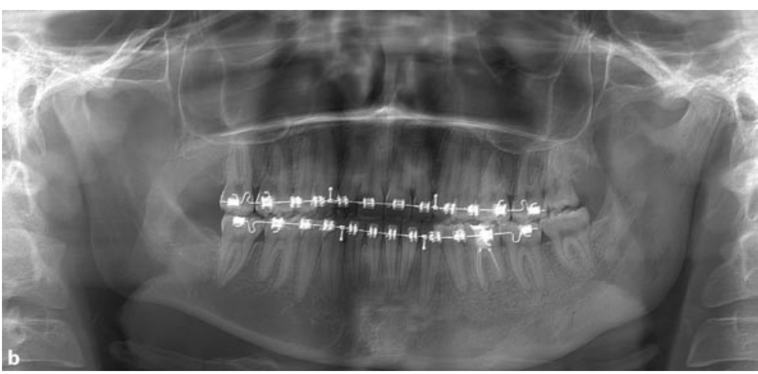
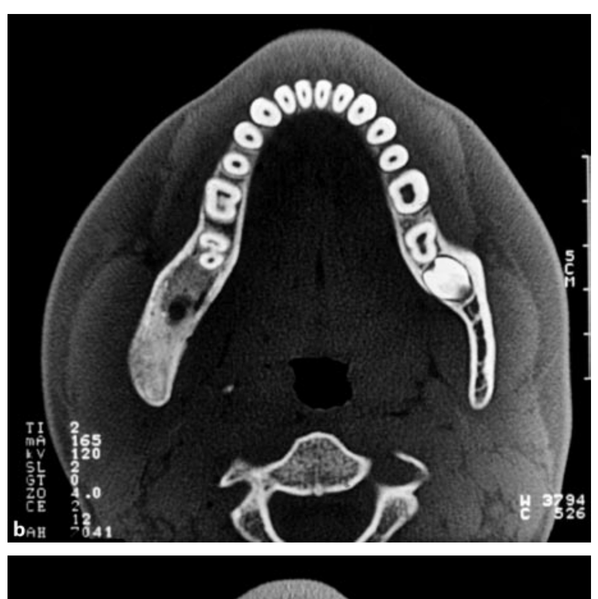


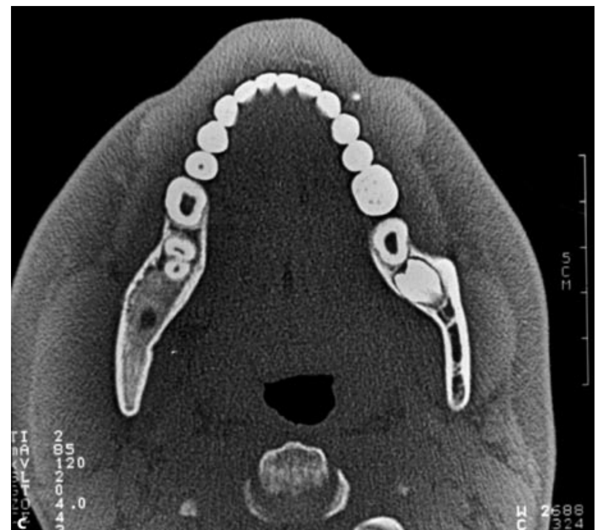
Fig. 8.22a–f Early-onset primary chronic osteomyelitis, 2 years follow-up. The soft tissue swelling is practically absent, whereas a residual bone deformity remains imposing as a surplus of bone tissue in the affected left mandible (**a**). **c–f** *see next page*

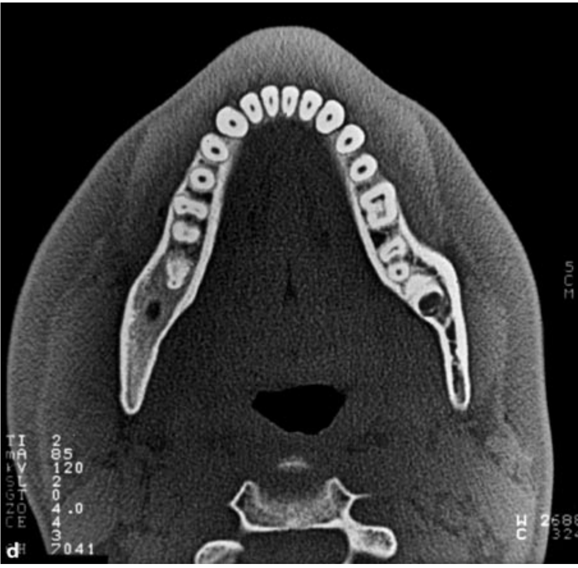


Fig. 8.22a–f (*continued*) The patient, however, did not experience any clinical symptoms for more than 2 years. The conventional radiographs which demonstrate the enlarged left mandibular corpus/angle and ascending ramus (**b–d**). Corresponding CT scans (**e,f**). (This case is described in detail in Chap. 12, case report 16.)









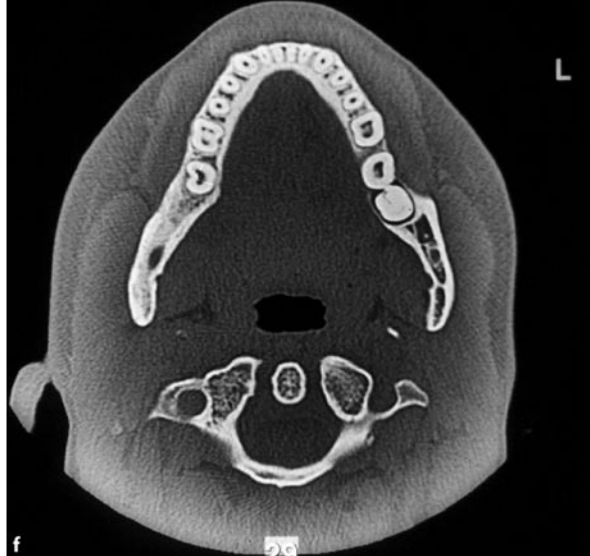


Fig. 8.23a–f Early-onset primary chronic osteomyelitis: Initial radiological findings at age 13 years show enlargement of the left mandibular corpus and angle with predominant sclerosis and some regions of osteolytis (**a**,**b**). Same patient 1 year later after conservative (nonsurgical) therapy (40 sessions HBO, 3 months antibiotic therapy): Bony architecture is returning to normal, with persisting predominant sclerosis and some regression of osteolytic lesions (**c**,**d**). **e**,**f** *see next page*



Fig. 8.23a–f (*continued*) Follow-up imaging studies after 4 years: further restoration of bony architecture, persisting sclerosis. The osteolytic lesions have disappeared (**e,f**)

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Osteomyelitis Therapy – Antibiotic Therapy

Werner Zimmerli

Contents

9.1 Summary

The principles of osteomyelitis therapy of the jaws are focus eradication by meticulous debridement including removal of dead bone and unstable internal fixation devices, combined with correct empirical and adequate antimicrobials. The most frequent microorganisms are viridans streptococci, peptostreptococci, *Eikenella corrodens*, *Fusobacterium* spp., and *Actinomyces* spp. In case of implant-associated osteomyelitis, *S. aureus* and coagulase-negative staphylococci are the most important infecting agents. Accordingly, empirical therapy should include the spectrum of these microorganisms. This is the case for amoxicillin/clavulanic acid or clindamycin. Acute osteomyelitis of neonates and young infants should be treated by the i.v. route for the first couple of days, followed by a 3- to 6-week oral treatment course. Acute osteomyelitis associated with trauma or fracture is treated for 6 weeks in the absence, and for 3 months in the presence, of an internal fixation device. In implant-associated staphylococcal infection, a rifampin combination, mostly a quinolone, should be preferred. In secondary chronic osteomyelitis therapy includes meticulous debridement surgery and long-term antibiotic therapy. Acute odontogenic and post-extraction osteomyelitis is sometimes caused by *Actinomyces* spp. These microorganisms are difficult to detect; therefore, biopsies instead of swabs are required, and the laboratory needs to be notified when submitting samples for culture. The duration of therapy is longer in actinomycosis, namely not only 4–6 weeks as in other types of osteomyelitis, but at least 6 months. True osteomyelitis arising from periimplantitis is rare despite exposure of the dental implants to the mouth flora and periodontal pathogens and must be treated by removal of the implant and eradication of necrotic bone tissue.

The therapy of primary chronic osteomyelitis remains controversial since the etiology and pathogenesis of this rare disease are not yet understood. A bacterial cause is discussed by some authors but has not been proven; hence, the role of antibiotic therapy in these cases is unclear.

9.2 General Aspects of Antibiotic Therapy in Bone Infection

The treatment goal in patients with osteomyelitis is to completely eradicate microorganisms and to support healing (Lew and Waldvogel 1997, 2004). This aim cannot always be reached in osteomyelitis of the jaws, because of the presence of teeth and persistent exposure of bone to microorganisms from the oral cavity. General principles of osteomyelitis therapy of the skeleton and the jaws are similar: focus eradication, meticulous debridement, including removal of dead bone and unstable internal fixation devices, if present, as well as application of correct empirical and adequate microorganism-directed antimicrobials (Trampuz and Zimmerli 2006a,b). In order to get an optimal treatment outcome with the least drawbacks, the interdisciplinary planning of the management of osteomyelitis is important. This should include the microbiologist, the infectious disease specialist, as well as the maxillofacial surgeon. This approach allows considering special requirements for microbiological diagnosis, correct antimicrobial therapy, and adequate debridement surgery.

Different types of osteomyelitis require different management strategies. In acute hematogenous osteomyelitis, antibiotic treatment is the most important pillar, and surgery is usually not required (Lew and Waldvogel 1997, 2004) or may be reduced to removal of the infectious focus and a minor debridement. In contrast, in (secondary) chronic osteomyelitis, healing cannot be achieved without a meticulous debridement including sequestrectomy, removal of necrotic bone including elimination of the focus and dead-space management, depending on the location of the infection (Trampuz and Zimmerli 2006a,b). As a rule, antimicrobial treatment of osteomyelitis in general should ideally be based on unambiguous microbiological results. This is also advocated in osteomyelitis of the jaws, since various microorganisms, including fungal agents or mycobacteria, can be involved (Bar et al. 2005; Bhatt and Jayakrishnan 2001; Dimitrakopoulos et al. 2005; Edelstein et al. 1993; Hovi et al. 1996; Sieber et al. 1977); thus, for efficacious antimicrobial therapy, culture and susceptibility testing is required. Since even in hematogenous osteomyelitis blood cultures are positive in only a minority of the cases, diagnostic biopsies are often necessary. In cases of sinus tracts or open wounds, superficial and even deep swabs may be misleading, since microorganisms from the soft tissue do not strongly correlate with those in the bone. Furthermore, contamination with normal resident flora may especially be misleading in specimens harvested through an enoral approach; therefore, if no bone biopsy can be sampled, empirical antimicrobial therapy against the most probable microorganisms is better than treatment based on culture results from open wounds. According to different studies, viridans streptococci, pyogenic streptococci, peptostreptococci, and bacteria from the HACEK group (*Haemophilus* spp., *Actinobacillus* spp., *Cardiobacterium* spp., *Eikenella corrodens and Kingella kingae), Propionibacterium acnes, Bacteroides* spp., *Fusobacterium* spp., *Actinomyces* spp., and *Staphylococcus aureus* are the most important microorganisms (Baker and Fotos 1994; Koorbusch et al. 1992; Taher 1993). In addition, in hospitalized people with comorbidity and in pretreated patients, Gram-negative bacilli, such as *Escherichia coli, Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, may also play a role (Ortqvist et al. 1990).

9.3 Special Requirements for Antibiotics Used in Osteomyelitis

In cases of acute osteomyelitis, antibiotic treatment does not differ from other deep-seated infections or sepsis. High-dose therapy with a bactericidal antibiotic for about 6 weeks is required (Lew and Waldvogel 1997, 2004). With all betalactams, high-dose signifies intravenous therapy, since the tolerance of oral betalactam precludes very high doses and the oral bioavailability is limited. In contrast, with quinolones, clindamycin, metronidazole, fusidic acid, trimethoprim/sulphametoxazole and rifampin, serum and tissue levels are similar whether these agents are given orally or by the i.v. route.

In extravascular infections, tissue penetration is considered as an important factor predicting elimination of the infective agent (Kuehnel et al. 2005); however, bone concentrations of antibiotics have not been shown to correlate with clinical outcomes in humans (Darley and MacGowan 2004). This has mainly technical reasons leading to variability due to sampling technique (e.g., limb ischemia due to tourniquet), blood contamination of the specimens, and type of samples (cortical vs. medullary bone). These variables make meaningful interpretation impossible (Davis 2005); thus, bone penetration should not be considered as an important argument in favor or against the use of the antimicrobial agent in patients with osteomyelitis. Data from animal models or clinical studies are more important. Yet, in

clinical studies, a follow-up period of at least 1–2 years is required to judge the efficacy of a specific regimen. Unfortunately, this requirement is rarely fulfilled in many company-sponsored drug-testing studies.

As a general rule in management of infectious diseases, the narrowest possible spectrum of antibiotics should be used, in order to avoid significant alterations of the normal mucosal flora with a shift to multiresistant microorganisms and fungal agents. Since narrow-spectrum antibiotics can only be used in microbiologically well-defined osteomyelitis, sampling of biopsies for culture ideally should precede antimicrobial therapy. Unfortunately, harvesting deep tissue samples may be surgically demanding in some cases, and therefore it is often combined with debridement procedure, dictating a different order of proceeding. Fusidic acid or rifampin should not be used as single agent, in order to avoid emergence of resistance.

Secondary chronic osteomyelitis of the jaws is defined as infection of more than 1-month duration. In this situation, antibiotic therapy must usually be combined with sufficient debridement surgery (e.g., decortication, partial resection if necessary). Surgery is mainly required for removal of necrotic bone, and bringing well-perfused vital tissue adjacent to the site of infection. The former is important since bacteria tend to persist on the surface of dead bone (Ciampolini and Harding 2000; Fux et al. 2005; Gristina et al. 1985; Stewart 2002). Persistence is caused by bacterial adherence to bone. Bacteria have similar properties, whether they adhere to foreign devices (implants) or to dead bone. Adherent bacteria are in the stationary phase of growth (Widmer et al. 1990, 1991; Zimmerli et al. 1994). This explains their phenotypic resistance to many antibiotics. The antibacterial efficacy of Betalactams on non-growing bacteria is limited, since they interfere with cell wall synthesis, which does not take place during stationary phase. In secondary chronic osteomyelitis, especially in cases associated with an infected implant, transplant, or foreign body, antibiotics need to act on stationary-phase bacteria. This is the case for quinolones against Gram-negative aerobes and for rifampin or clindamycin against staphylococci (Widmer et al. 1990, 1991; Zimmerli et al. 1994). The excellent efficacy of clindamycin monotherapy and rifampin combination therapy in secondary chronic osteomyelitis due to *S. aureus* has been shown in a rabbit model (Norden 1988; Norden et al. 1983, 1986).

In cases of secondary chronic osteomyelitis associated with an infected implant, transplant, or foreign body, adherence of microorganisms and biofilm formation is an important pathogenetic mechanism (Darouiche 2001; Trampuz and Zimmerli 2005). The biofilm acts as a sanctuary site protecting microorganisms from antimicrobial agents and host defense (Stewart 2002; Trampuz and Zimmerli 2005). In such cases, the removal and replacement and of the implant/transplant should always be considered; otherwise; the same therapeutic principles as mentioned above must be respected. In cases of staphylococcal infection, treatment with rifampin combined with either a quinolone, or clindamycin, or fusidic acid or trimethoprim/sulfamethoxazole, is the best option (see below; Zimmerli et al. 2004). Clindamycin should be preferred against anaerobes, and quinolones are the best choice against *Enterobacteriaceae* due to their good bioavailability and their efficacy on stationary-phase Gram-negative bacilli (Andriole 2005; Fluckiger and Zimmerli 2004; Lew and Waldvogel 2004).

9.4 Antibiotic Treatment According to the Different Types of Osteomyelitis of the Jaws

9.4.1 Acute Osteomyelitis in Neonates and Young Infants (Neonatal, Tooth-germ-associated Acute Osteomyelitis)

This is a rare form of osteomyelitis which normally occurs in children mainly below the age of 2 years (Loh and Ling 1993). It usually results from hematogenous seeding from a distant focus such as pneumonia or upper respiratory tract infection. This localization of hematogenous osteomyelitis has not been observed in adults. In addition, according to a MEDLINE search, this entity has almost disappeared during the past 30 years (Adekeye and Cornah 1985; Nelson 1991). This is most likely explained by the fact that most bacterial infections are rapidly treated with antimicrobial agents; thus, hematogenous seeding in the bone has become very rare in neonates and infants. Acute osteomyelitis of the jaw begins with sudden local swelling, and fever. Later, it is complicated by increased mobility of the teeth in the involved area, abscess formation, and possible rapid spreading into adjacent areas such as the orbit, nasal, and oral cavity.

In cases of early diagnosis, no surgical treatment is usually required. In cases of teeth involvement, extraction of the dental focus is advisable; however, in subacute cases which have not rapidly been treated, addi-

tional surgical treatment of abscesses and removal of necrotic bone may be unavoidable.

Before starting the initial empirical antibiotic therapy, at least two pairs of blood cultures should be drawn. If a lower or upper respiratory tract infection is the primary source, treatment with amoxicillin/clavulanic acid (55 mg/kg i.v. every 6 h) or clindamycin (7.5 mg/kg i.v. every 6 h) is adequate. In case of sepsis with unknown primary focus, *S. aureus* is the most important microorganism. Treatment depends on the local epidemiology. If the prevalence of methicillin-resistant *S. aureus* (MRSA) is low, amoxicillin/clavulanic acid, flucloxacillin (50 mg/kg i.v. every 6 h) or cefuroxime (50 mg/kg i.v. every 8 h) are good choices. In case of high prevalence of MRSA, vancomycin (50 mg/kg i.v. every 6 h) should be administered. If the primary focus is meningitis, the use of cefotaxime (75 mg/kg every 6 h) or ceftriaxone (100 mg/kg once daily) is proposed. As soon as the microorganism is known, treatment should be optimized according to the results of the susceptibility testing.

The duration of treatment is not standardized based on comparative studies. However, extrapolating to cases of acute osteomyelitis in other localization, there is a risk of recurrence or transition to secondary chronic osteomyelitis, if antibiotics are given only for a short time; therefore, as a rule, high-dose antibiotic therapy should be given for up to 6 weeks in such instances (Murry 2005). However, in children shorter treatment duration is suggested by some authors. Steer and Carapetis (2004) recommend 3 days of intravenous therapy followed by 3 weeks of high-dose oral antimicrobial agents, provided there is no underlying illness, the presentation is typical and acute, and there has been a good response to treatment. The initial treatment is generally given by the i.v. route. If no drug with good bioavailability is available, the i.v. treatment should be continued for at least 3 weeks. If the microorganism is susceptible to clindamycin, trimethoprim/sulfamethoxazole or quinolones, these agents can be given by the oral route, as soon as the acute sepsis syndrome is controlled, provided that compliance of the patient is guaranteed. The use of quinolones in children is now considered as safe (Schaad 2005); thus, in case of a solid indication, these drugs (e.g., ciprofloxacin 20–30 mg/kg every 12 h) can be also given to infants and children.

9.4.2 Trauma/Fracture-related Acute Osteomyelitis

This type of osteomyelitis occurs at any age. Microorganisms are inoculated by the exogenous route. Since fractures of the upper and especially the lower jaw in dentate patients often communicate with the periodontium, and hence the oral cavity, these fractures should always be considered as open. In these cases the identified microorganisms are those of the normal oral flora. In contrast to hematogenous osteomyelitis, *S. aureus* is rarely the cause of trauma/fracture associated osteomyelitis of the jaws (Hudson 1993). *S. aureus* and other members of the skin flora, however, should be considered if the fracture communicates with extraoral soft tissue and skin as frequently seen in severe facial trauma with soft tissue laceration. In most cases, the disease is polymicrobial, including streptococci, *Fusobacterium nucleatum, Bacteroides* spp., and other microorganisms from the oral cavity. Very rare cases can be caused by *Actinomyces* spp.; however, this microorganism mainly causes odontogenic osteomyelitis (see below; Smego and Foglia 1998). If osteomyelitis occurs after osteosynthesis of the bone, coagulase-negative staphylococci and *S. aureus* are the most frequently observed microorganisms (Trampuz and Zimmerli 2006a,b).

Table 9.1 summarizes the antimicrobial therapy against the most frequent microorganisms involved in osteomyelitis of the jaws. The duration of treatment is 6 weeks, in order to minimize the risk for persistence and recurrence. Since microorganisms adhere to implants or other hardware, infections involving osteosynthesis usually require a longer duration of treatment (Stewart and Costerton 2001). Analogous to treatment of such infections at other locations, a 3-month therapy may be more safe (Zimmerli et al. 1998). Rifampin combined with a quinolone, fusidic acid or trimethoprim/sulfamethoxazole has been shown to have good activity on implant-adhering staphylococci (Drancourt et al. 1993; Trampuz and Zimmerli 2006a,b; Zimmerli et al. 1998, 2004). Therefore, a rifampin combination should be preferred in such infections; however, the use of rifampin is only indicated if the bone fixation has no open communication to the surface. Otherwise, the osteosynthesis material would be rapidly colonized by rifampin-resistant microorganisms from the mouth flora. In such cases, as mentioned previously, removal or replacement of the implants is a *conditio sine qua non* combined with sufficient soft tissue coverage.

9.4.3 Trauma/Fracture-related Secondary Chronic Osteomyelitis

If acute osteomyelitis is not rapidly diagnosed and treated with the correct antibiotic for a prolonged time, secondary chronic osteomyelitis occurs. As a rule, this

Table 9.1 Antibiotic treatment of osteomyelitis of the jaws caused by common microorganisms (Modified according to Zimmerli et al. 2004)

Microorganism	Antimicrobial agent	Dose	Route
Staphylococcus aureus or coagulase-negative staphylococci			
Methicillin-susceptible	Flucloxacillin[1]	2 g every 6 h	IV
	+ Rifampin	450 mg every 12 h	PO/IV
	for 2 weeks, followed by		
	Ciprofloxacin	750 mg every 12 h	PO
	or Levofloxacin	500 mg every 12 h	PO
	each + Rifampin	450 mg every 12 h	PO
Methicillin-resistant	Vancomycin	1 g every 12 h	IV
	+ Rifampin	450 mg every 12 h	PO/IV
	for 2 weeks, followed by		
	Ciprofloxacin[2]	750 mg every 12 h	PO
	or Levofloxacin[2]	500 mg every 12 h	PO
	or Teicoplanin[3]	400 mg every 24 h	IV/IM
	or Fusidic acid	500 mg every 8 h	PO
	or Cotrimoxazole	1 DS tablet every 8 h	PO
	or Minocycline	100 mg every 12 h	PO
	each + Rifampin	450 mg every 12 h	PO
Streptococcus spp.	Penicillin G	5 million U every 6 h	IV
	or Ceftriaxone	2 g every 24 h	IV
	for 4 weeks, followed by		
	Amoxicillin	750–1000 mg every 8 h	PO
Enterococcus spp. (penicillin-susceptible)	Penicillin G	5 million U every 6 h	IV
	or Ampicillin or Amoxicillin	2 g every 4–6 h	IV
	+ Aminoglycoside		IV
	for 4 weeks, followed by		
	Amoxicillin	750–1000 mg every 8 h	PO

The antimicrobial susceptibility of the pathogen needs to be determined before treatment. The antimicrobial dose is given for adults with normal renal and hepatic clearance. PO = orally; IV = intravenously; IM = intramuscularly; DS = double-strength (Trimethoprim 160 mg, Sulfamethoxazole 800 mg).

1 In patients with delayed hypersensitivity, cefazolin (2 g every 8 hr IV) can be administered. In patients with immediate hypersensitivity, betalactam should be replaced by vancomycin (1 g every 12 hr IV).

2 Methicillin-resistant Staphylococcus aureus should not be treated with quinolones since antimicrobial resistance may emerge during treatment.

3 Initial loading dose is 800 mg/d IV (first day)

4 Alternatively, penicillin G or ceftriaxone can be used for gram-positive anaerobes (e.g. Propionibacterium acnes), and metronidazole (500 mg every 8 hr IV or PO) for gram-negative anaerobes (e.g. Bacteroides spp.).

Table 9.1 (*continued*)Antibiotic treatment of osteomyelitis of the jaws caused by common microorganisms (Modified according to Zimmerli et al. 2004)

Microorganism	Antimicrobial agent	Dose	Route
Enterobacteriaceae (quinolone-susceptible)	Ciprofloxacin	750 mg every 12 h	PO
Nonfermenters (e.g *Pseudomonas aeruginosa*)	Ceftazidime or cefepime + aminoglycoside for 2 to 4 weeks, followed by Ciprofloxacin	2 g every 6 h 750 mg every 12 h	IV IV PO
Anaerobes[4]	Clindamycin for 2 weeks, followed by Clindamycin	600 mg every 6–8 h 300 mg every 6 h	IV PO
Mixed infections (without Methicillin-resistant staphylococci)	Amoxicillin/clavulanic acid or Ampicillin/Sulbactam Carbapenem for 2 to 4 weeks, followed by individual regimens according to antimicrobial susceptibility	2.2 g every 8 h 3 g every 8 h According to compound	IV IV IV

The antimicrobial susceptibility of the pathogen needs to be determined before treatment. The antimicrobial dose is given for adults with normal renal and hepatic clearance. PO = orally; IV = intravenously; IM = intramuscularly; DS = double-strength (Trimethoprim 160 mg, Sulfamethoxazole 800 mg).

1 In patients with delayed hypersensitivity, cefazolin (2 g every 8 hr IV) can be administered. In patients with immediate hypersensitivity, betalactam should be replaced by vancomycin (1 g every 12 hr IV).

2 Methicillin-resistant Staphylococcus aureus should not be treated with quinolones since antimicrobial resistance may emerge during treatment.

3 Initial loading dose is 800 mg/d IV (first day)

4 Alternatively, penicillin G or ceftriaxone can be used for gram-positive anaerobes (e.g. Propionibacterium acnes), and metronidazole (500 mg every 8 hr IV or PO) for gram-negative anaerobes (e.g. Bacteroides spp.).

type of osteomyelitis cannot be treated with antibiotics alone. Before antibiotic treatment, meticulous debridement surgery, usually decortication of the bone, including the excision of all dead tissue and lavage/drainage of pus is required accompanied by adequate (re)fixation of the fracture. During this surgery, at least three biopsy samples for anaerobic and aerobic culture are desirable. If *Actinomyces* spp. is suspected, the laboratory must be informed in advance, since a prolonged (4 weeks) and strictly anaerobic incubation is mandatory. Immediately after sampling of the biopsies, i.v. treatment with an antibiotic acting on microorganisms from the mouth flora should be started. Amoxicillin/clavulanic acid (2.2 g i.v. every 6 h) or in case of delayed type penicillin allergy, ceftriaxone (2 g i.v. once daily) are good choices. If a patient has a history of a penicillin allergy of an immediate type, clindamycin (600 mg i.v. every 8 h or 400 mg pos every 6 h) can be given. This treatment should be optimized as soon as the microbiology results are available.

The duration of treatment of secondary chronic osteomyelitis is not standardized. It mainly depends on the duration and extent of the infection, the velocity of the clinical and laboratory response to treatment, the

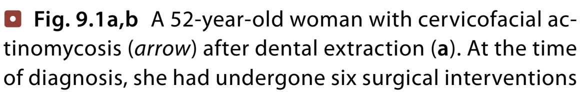


Fig. 9.1a,b A 52-year-old woman with cervicofacial actinomycosis (*arrow*) after dental extraction (**a**). At the time of diagnosis, she had undergone six surgical interventions without success. A CT scan of the same patient (**b**). Severe tumor-like soft tissue swelling is typically visible

presence of an implant, and the quality of the initial debridement surgery. In general, antibiotics should be given between 6 weeks and 3 months; thus, a drug with good oral bioavailability should be chosen. According to animal data, clindamycin is a good choice in secondary chronic osteomyelitis due to *S. aureus* (Norden 1988; Norden et al. 1983, 1986). By extrapolation, this regime is also preferred for long-term therapy of other types of secondary osteomyelitis caused by susceptible microorganisms.



Fig. 9.2 A 23-year-old women with cervicofacial actinomycosis after dental extraction. Diagnosis was made with an anaerobic culture from tissue sampled at the first and only debridement surgery

9.4.4 Acute Odontogenic Osteomyelitis (Including Actinomycosis)

The management of acute odontogenic osteomyelitis does not differ from that of acute osteomyelitis attributed to trauma or fracture; however, in this type of osteomyelitis, *Actinomyces* spp. is a common infectious agent. The microbiological diagnosis of this infection is difficult but very important. The presence of *Actinomyces* spp. in the culture does not prove actinomycosis, since it may be just a colonizing microorganism. The clinical characteristics of actinomycosis include prolonged infection, fistula formation, "sulfur granules" in exudates or tissues, and a "woody" hard swelling at the site of infection (Figs. 9.1, 9.2; Nagler et al.1997). The diagnostic yield can be optimized if the following requirements are considered: (1) bone or soft tissue biopsies using a strict protocol to avoid contamination are preferred over swabs; (2) favorable transport conditions for the specimen (anaerobic transport medium, if immediate culture is not feasible); (3) a high degree of clinical suspicion in order to inform the microbiologist in advance (>3-week incubation required). In case of lack of suspicion or lack of microbiological knowledge, diagnosis and adequate treatment may be delayed by several months (Bartkowski et al. 1998). According to a recent review, cervicofacial actinomycosis may extend to the underlying mandible or facial bone (Smego and Foglia 1998). In a patient from our own series, actinomycosis was diagnosed after she had undergone six surgical interventions (incision, drainage, sequestrectomy) subsequent to a dental extraction, before adequate sampling biopsies allowed the final diagnosis (Fig. 9.1). Interestingly, in almost all cases of cervicofacial actinomycosis, multiple anaerobic and aerobic microorganisms are simultaneously present (Marx et al. 1994; Robinson et al. 2005; Smego and Foglia 1998). Nevertheless, the antimicrobial therapy must not be directed against concurrently cultured microorganisms as part of a polymicrobial flora. Regimens that target only *Actinomyces* spp. are generally curative.

In cases of acute odontogenic osteomyelitis when soft tissue necrosis or abscesses have not yet developed, minor surgical debridement with removal of the dental focus combined with antimicrobial therapy may be efficacious. In contrast, in secondary chronic osteomyelitis, a more extensive surgical debridement (e.g., decortication) is an essential part of the treatment (see below). In case of unspecific polymicrobial etiology, amoxicillin/clavulanic acid or a carbapenem are good choices (Table 9.1). The duration of treatment is 4–6 weeks. In case of actinomycosis, penicillin G (20 million U/day i.v. in four doses) is the treatment of choice. In case of penicillin allergy, clindamycin or a cephalosporin (e.g., ceftriaxone 2 g/day i.v.) are alternatives. After a duration of 2 weeks, it can be switched to an oral regimen which should be continued for at least 6 months (Smego and Foglia 1998). We prefer clindamycin (4×300 mg/day per os), because it has a better bioavailability than penicillin V. Amoxicillin (3×750 mg/day per os), which has a better bioavailability than penicillin V, or a tetracyclin (doxycycline 200 mg/day per os) are also efficacious.

9.4.5 Odontogenic Secondary Chronic Osteomyelitis

The limit between acute and secondary chronic osteomyelitis is fluent and can only be arbitrary defined with a clear-cut time interval after beginning of the deep bone infection. As in osteomyelitis of other localization, osteomyelitis of the jaws can persist for several years and symptomatically appear at any time during life (Ertas et al. 2004; Widmer et al. 1988). According to Marx (1991), the arbitrary limit differentiating acute from secondary osteomyelitis of the jaws is 1 month. This time limit demonstrates the refractoriness to host defense and initial therapy. Regarding therapy, the crucial difference lies in the absence or presence of major osteolysis, bone sequesters, and periosteal reactions which should be sought with CT scans or MR images; thus, the cornerstone of an efficacious treatment is a meticulous surgical debridement including removal of the dental focus. This procedure should always be combined with biopsies for microbiological cultures and histology. After sampling, antimicrobial treatment with i.v. amoxicillin/clavulanic acid, or carbapenem in case of penicillin allergy or failure of previous treatment, should be started (for dose see Table 9.1). After an initial 2-week treatment by the i.v. route, an oral substance with good bioavailability should be chosen according to the microbiology of the initial biopsy samples (see Table 9.1). In analogy to the good efficacy of clindamycin in chronic staphylococcal osteomyelitis, this drug is also a good choice in cases of secondary chronic odontogenic osteomyelitis of the jaws (Norden et al. 1986; Xue et al. 1996). The duration of treatment is 6 weeks up to 6 months, in some studies shorter (4 weeks). In the large series of Kim and Jang (2001), the outcome of 49 patients with secondary chronic osteomyelitis of the jaws was analyzed. The success rate in 39 patients with surgery and 8 weeks of antibiotics (2 weeks of i.v. and 6 weeks of per os) was 94.9% as compared with 60% in 10 patients with surgery alone.

The duration of treatment is not defined by comparative studies. It is based on expert opinions. Arguments for a very long treatment are the presence of *Actinomyces* spp., the presence of an implant (see below), incomplete debridement, or a duration of infection of several years. In such cases with a prolonged and complicated course repeated surgery is often necessary and adjunctive hyperbaric oxygen therapy may be advisable.

Furthermore, the continuing rising costs in health care force us to revaluate expensive therapies such as long-term i.v. antibiotics, which mostly require an inpatient treatment; hence, evidence-based protocols based on prospective multicenter trials concerning the duration and application route of antibiotics in acute and secondary chronic osteomyelitis of the jaws are mandatory.

9.4.6 Foreign Body, Transplant/Implant-induced Acute Osteomyelitis

The antibiotic treatment is very different, whether the patient suffers from infection of a transplant/internal fixation device or from periimplantitis related to dental implants. In transplant/implant-associated osteomyelitis, the transplant/implant is in a closed compartment, and the surgical and antibiotic treatment aims to sterilize the infectious focus. In contrast, in cases of periimplantitis related to a dental implant, the implant is in an open compartment, i.e., in permanent contact with the oral microflora; thus, the aim of the treatment is to reduce bone inflammation, not to eliminate the implant-associated microorganisms.

In cases of osteomyelitis attributed to osteosynthesis material, the treatment principles do not differ from those in other parts of the body (Trampuz and Zimmerli 2006a,b). Antibiotic therapy should always be combined with a meticulous surgical debridement usually including the replacement or removal of the contaminated plates and screws.

Infections associated with subcutaneous plate fixations usually produce clinical symptoms within a few days or weeks. Early infections (<2 weeks) are mainly caused by *S. aureus* or Gram-negative bacilli, delayed infection (3–10 weeks) by microorganisms of low virulence, mainly coagulase-negative staphylococci. Such infections can generally be treated without removal of the hardware. Suggested antimicrobial treatment according to the pathogen and its susceptibility is summarized in Table 9.1 (Zimmerli and Ochsner 2003; Zimmerli et al. 2004). Intravenous treatment should be administered for the first 2–4 weeks, followed by oral therapy for a total of 3 months if the implant is not removed. Rifampin can eliminate surface-adhering staphylococci, and quinolones surface-adhering Gram-negative bacilli, allowing to cure implant-associated infections without removal of the hardware (Widmer et al. 1990, 1991; Zimmerli et al. 1994, 1998, 2004). In many situations, treatment with implant retention is only suppressive, operating until the implant can be removed. In such cases, antibiotics should be discontinued at least 2 weeks before removing the implant, in order to get reliable intraoperative tissue specimens for culture. If tissue cultures are still positive, antimicrobial treatment should be continued for about 4–6 weeks after implant removal to prevent further chronification of osteomyelitis (Table 9.1).

Dental implants are exposed to and colonized by microorganisms from the normal flora and/or by putative periodontal pathogens. The predominant flora in successful dental implants includes *Streptococcus oralis, Eubacterium nodatum, Veillonella parvula*, and *Actinomyces naeslundi*. In failing implants, the predominant culturable microorganisms are different, namely, *Streptococcus intermedius, Bacteroides forsythus, Campylobacter gracilis, Fusobacterium nucleatum*, and *Porphyromonas gingivalis* (Leonhardt et al. 2003; Tanner et al. 1997). Since dental implants, especially those with a rough surface, cannot be sterilized in situ, antimicrobial therapy can only limit inflammation and infection around the device. Unfortunately, there are no controlled clinical trials regarding antibiotic treatment of periimplantitis. In two comprehensive reviews, various aspects of the treatment of periimplant infections are summarized (Klinge et al. 2002; Roos-Jansaker et al. 2003). For surgical interventions and local treatment, several reviews can be consulted (Klinge et al. 2002; Roos-Jansaker et al. 2003; Schou et al. 2004). According to Klinge et al. (2002), the treatment regimens regarding the type of antibiotic, dosage, and duration are so different that the clinical benefit of a specific antimicrobial therapy cannot be judged, and it can even be questioned. In cases of severe periimplantitis, antibiotic therapy with either amoxicillin/clavulanic acid (625 mg/8 h) or clindamycin (300 mg/6 h) should be given by the oral route during 7–10 days (Klinge et al. 2002; Roos-Jansaker et al. 2003; Sanchez-Garces and Gay-Escoda 2004). In several studies, ornidazole, metronidazole, cotrimoxazole, or ciprofloxacin have been given (Leonhardt et al. 2003; Mombelli and Lang 1992; Wetzel at al. 1999). In view of the involved microorganisms, this is not an optimal choice, since streptococci and *Actinomyces* spp. are not susceptible to these antibiotics.

9.4.7 Foreign Body, Transplant/Implant-induced Secondary Chronic Osteomyelitis

If acute or delayed transplant/implant-associated infection is not adequately treated, secondary chronic osteomyelitis may occur. Generally, such infection cannot be cured without removal of all hardware and/or transplant. Removal of the implants and surgical debridement are the first steps, followed by a 6- to 12-week course of oral antibiotics according to the susceptibility of the microorganism (Table 9.1). If the infecting agents are unknown, the combination of clindamycin (300 mg/6 h per os) plus ciprofloxacin (750 mg/12 h per os) is a good empirical choice.

Untreated periimplantitis may eventually lead to deep bone invasion and hence cause true osteomyelitis; however, compared with the large amount of dental implants placed today this remains a rare complication. In such instances of acute and secondary chronic osteomyelitis associated with a dental implant, removal of the implant alone must be accompanied by a meticulous surgical debridement of the infected and necrotic bone tissue, while plane periimplantitis without osteomyelitis always resolves once the implant is removed and local curettage performed.

9.5 Primary Chronic Osteomyelitis

Primary chronic osteomyelitis is a chronic bone inflammation of unknown origin. It is characterized by the lack of pus formation, sequesters, and fistula formation (Baltensperger et al. 2004; Eyrich et al. 2003). It is still unclear whether this disease is caused by bacterial infection or by an immunological disorder (Farnam et al. 1984; Flygare et al. 1997). In the comprehensive case series of Baltensperger et al. (2004), in 3 of 21 examined cases no bacterial growth could be detected. In bone specimens of 18 cases, cultures grew various types of bacteria, all corresponding to the normal flora of the oral cavity. Thus, these microorganisms could be either contaminants from samples harvested through the oral mucosa, or true infecting agents causing chronic inflammation. Many arguments favor the former hypothesis:

1. In most samples from primary chronic osteomyelitis in long bones no bacterial growth can be detected (Carr et al. 1993).
2. The lack of pus and fistula (Baltensperger et al. 2004).
3. The coexistence of this entity with immunological characteristics such as the SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis) syndrome (Eyrich et al. 1999).
4. The histology with the lack of neutrophils, predominant sclerosis, and periosteal new bone formation (Eyrich et al. 2003).

Unfortunately, there is no single study which shows a convincing effect of antimicrobial therapy. In most case series, all patients were treated with antibiotics (Baltensperger et al. 2004; Eyrich et al. 2003; Flygare et al. 1997; Jacobsson and Hollender 1980); however, no concept regarding the type of antibiotics or duration is visible. A controlled study will probably never be possible, since this disease is very rare and most clinicians are reluctant not to treat with antibiotics, mainly for liability reasons. There are even no data comparing short-term vs. long-term antibiotic therapy.

As long as no studies are available, a single 1-month course of antibiotics against bacteria from the oral flora may be justifiable. Clindamycin (300 mg every 6 h) or amoxicillin/clavulanic acid (625 mg every 8 h) are a rational choice. Yet, prolonged or repeated courses should be avoided, if secondary chronic osteomyelitis is excluded. It should be kept in mind that all antibiotics have side effects which may harm the patient.

A reasonable alternative to antibiotic treatment studies would be a careful diagnostic trial. In such a study, biopsies should be sampled through a well-disinfected surface (preferable skin instead of mucosa) and analyzed not only by conventional culture but also by PCR technique. If bacterial etiology can be ruled out by such a study, antiinflammatory drugs and/or bisphosphonate therapy should be tested as a novel treatment concept; the latter, however, is known to have certain drawbacks such as a possible lifelong deposition in bony tissue and possible induction of osteochemonecrosis of the mandible (Badros 2006).

9.6 Follow-up controls

Due to the nature of the disease, patients with osteomyelitis of the jaws need careful and regular clinical and radiological follow-up visits during at least 2 years to evaluate therapy effectiveness and to rule out relapse of the disease. During the initial phase, clinical (local signs of inflammation, fever) and laboratory (C-reactive protein, leukocyte counts) signs of infection should be closely monitored. In acute osteomyelitis, persistent in-

fection may indicate inadequate antimicrobial therapy either due to wrong or missing microbiological data (superficial swab instead of deep biopsy), or due to an antimicrobial treatment with an insufficient drug (low bioavailability, unexpected resistance, emergence of resistance during therapy or superinfection).

In cases of primary chronic osteomyelitis of the jaws follow-up may be necessary for many years or even decades, since there is still no parameter which guarantees full recovery from this disease.

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Osteomyelitis Therapy – Hyperbaric Oxygen as an Adjunct in Treatment of Osteomyelitis of the Jaws

Jörg Schmutz

10

Contents

10.1 Summary

In craniofacial and head/neck infections, with or without bone involvement, surgery is the mainstay of treatment. Antibiotics are always used as adjuncts, although there are few studies documenting evidence of their efficacy in this setting. There is a large body of in-vitro and in-vivo experimental evidence which shows that hyperbaric oxygen (HBO) is able to counteract the deleterious effects of local hypoxia on infection and wound healing. Experimental data show that HBO has a direct antibacterial effect equivalent to antibiotics for strictly anaerobic bacteria. Other experimental data show an improvement of neutrophils mediated bacterial killing for *P. aeruginosa*, *S. aureus*, and *B. melaninogenicus*. In experimental

animal osteomyelitis, HBO compares favorably with the antibacterial effect of cephalosporins, gentamicin, amikacin, and tobramycin, showing even an additive effect. Clinical results confirm the experimental data, although controlled studies are still lacking. Hyperbaric oxygen seems to be associated with better survival in severe cervical necrotizing soft tissue infections. Hyperbaric oxygen allows a better infection demarcation in chronic osteomyelitis of the jaw. As a consequence, less major surgery seems to be required for infection control. Adjunctive HBO improves outcomes and reduces the need for surgical reintervention, and furthermore in some instances allows infection control without mandatory removal of foreign material. Hyperbaric oxygen, associated with standard care, has further been associated with improved survival as well as better infection control in zygomycosis (mucormycosis) of the older diabetic patient.

10.2 Definition of Hyperbaric Oxygen

According to a survey performed in the U.K. (Kanatas et al. 2005), most of the 125 maxillofacial consultants who were asked about hyperbaric oxygen (HBO) were neither aware of its mode of delivery nor of its mechanism of action. For this reason, the process of hyperbaric oxygenation is briefly described. Hyperbaric oxygen (HBO is defined in the European Code of Good Practice (http://www.oxynet.org/) as the inhalation of pure oxygen (FiO_2=1) under a pressure above the ambient pressure. Pressure is indicated in kilo Pascal (kPa) or in atmosphere absolute (ATA). A hyperbaric chamber is needed for this purpose. It is defined as a pressure vessel capable of accommodating one or more persons with the purpose of providing medical treatment. In medicine, HBO is used within the range of 100–300 kPa. Above this pressure, oxygen presents an increased risk of central nervous toxicity (Doherty and Hampson 2005). Two different types of HBO chambers are distinguished: the multiplace chamber, offering space for two or more patients, and the monoplace chamber, with space only for one person.

10.3 Hyperbaric Chambers

10.3.1 Multiplace, ICU Compatible HBO Chamber

Multiplace HBO chambers have at least two compartments. Larger ones may harbor space for several patients (Fig. 10.1a,b). According to their size, they can allow access of staff, patients, and various equipments into the chamber, while maintaining pressure in the main compartment. To cope with the requirements of very early postoperative HBO therapy, recently built hyperbaric chambers are designed as real hyperbaric ICU units (Fig. 10.1c). These chambers are usually located within the hospital's ICU and can accommodate patients in their hospital beds with all the necessary support of a modern ICU.

10.3.2 Monoplace HBO Chamber

Monoplace HBO chambers are single-compartment vessels designed for a single patient. Due to their limited space, they do not allow direct access to the patient during the treatment but can allow distance intensive care monitoring and respiratory assistance (Fig. 10.2).

10.3.3 Breathing Systems

Usually, patients in multiplace HBO chambers are required to breathe the pure oxygen through a tight face mask (Fig. 10.3).

In maxillofacial, ENT, and facial plastic surgery some patients are not able to wear such a mask because their face has just received surgery and/or they may have external fixation devices. A further obstacle of wearing a mask may be a concomitant tracheotomy, which is sometimes present in these patients. In such instances, specially designed and comfortable hoods have been created as seen in Fig. 10.4a.

10.4 Oxygen and Bacteria

For better explanation of the mechanisms in treating infections with HBO, it is necessary to understand the physiology of bacteria, according to their behavior when confronted with its presence or absence. Depending on their susceptibility to oxygen, bacteria can be divided into five major groups: (1) strictly aerobes; (2) microaerophils; (3) facultative anaerobes; (4) aero-tolerant anaerobes; and (5) strictly anaerobes. These groups are described as follows:

1. Strictly aerobes: These bacteria absolutely need oxygen because it is vital for them. In an oxygen-free en-

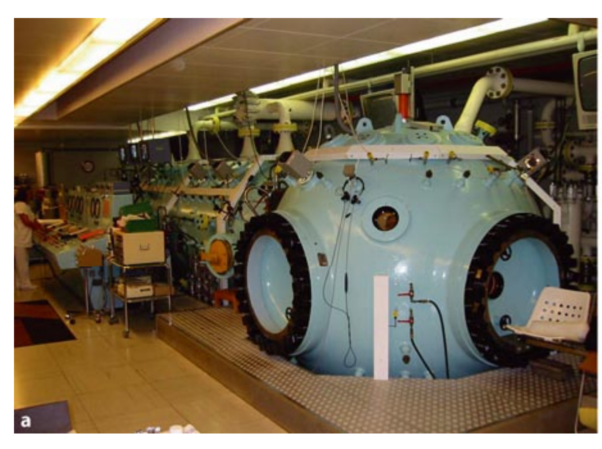






Fig. 10.1 **a** Multiplace hyperbaric oxygen chamber, University Hospital Zurich. **b** Inside view of the multiplace hyperbaric oxygen chamber, University Hospital Zurich: Patients can be seated or situated in a lying position if needed **c** Berufsgenossenschaftliches Trauma Zentrum Murnau, Germany: Multiplace hyperbaric oxygen chamber with integrated ICU facilities (Courtesy of H. Schöppenthau)



Fig. 10.2 Monoplace hyperbaric oxygen chamber with intensive care monitoring (Courtesy of P. Kuessel)



Fig. 10.3 Patient with a tight face mask breathing oxygen in a hyperbaric chamber





Fig. 10.4a,b Patient with oxygen tent breathing oxygen in a hyperbaric chamber: The neck is sealed with a latex membrane preventing oxygen from contaminating the chamber. Exhaled oxygen O_2 and CO_2 is also brought outside the chamber (**a**). Patient with tracheotomy (**b**, *arrow*): The sealing membrane is taped on the patient's shoulders. The head tent is then applied on the neck ring

vironment they cannot survive. Examples are *Neisseira* spp. and *Pseudomonas* spp.

2. Microaerophils: These bacteria, like *Helicobacter* spp. and *Campylobacter* spp., need oxygen, but they develop best in an environment with a partial pressure of oxygen inferior to air.
3. Facultative anaerobes: These bacteria, like *Staphylococcus* spp. or *Enterobacteriaceae* spp., can develop with or without of oxygen.
4. Aerotolerant anaerobes: These bacteria, like *Streptococci* spp. and *Enterococci* spp., can develop with or without oxygen but only in an environment with a low partial pressure of oxygen.
5. Strictly anaerobes: These bacteria can only develop without oxygen. Oxygen is lethal for them because they lack defensive enzymes such as superoxide dismutase, catalase, and peroxydase. Prominent examples of these bacteria are *Bacteroides* spp., *Clostridium* spp., or *Peptostreptococcus* spp.

10.5 Oxygen and Surgical Infection

In the clinical situation, oxygen delivery to the wound is most essential for infection control. Hopf et al. (1997) measured the partial pressure of oxygen (PO_2) in the subcutis of 131 patients operated in general surgery. They found an increased number of wound infections in tissues where a low partial oxygen pressure was measured (Table 10.1).

In another study, Belda et al. (2005) found a significant decrease in postoperative wound infections in colorectal surgery (39% decreases) in patients receiving supplemental oxygen. Patients who inspired 80% oxygen during and after surgery for 6 h had significantly less infection than control subjects who breathed only of 30% oxygen.

10.6 Oxygen and Host Defenses

Neutrophils are one of the main responsible blood cells for bacterial killing. For this purpose, they use oxygen-dependent and oxygen-independent mechanisms to kill phagocytosed bacteria. The oxygen-dependent mechanism is of particular interest regarding the effect of HBO and is considered to be the clinically the most significant one. It is therefore discussed more in depth. It is well known that impaired circulation, as found in older ages or in diabetic patients, leads to ischemia and decreased wound healing. This effect can somewhat be countered by HBO (Quirinia and Viidik 1996). Immunosuppressed patients also have an increased risk of infection due to impaired mechanism of host defenses (Dohil et al. 1997).

10.6.1 Host Defenses Are Decreased by Hypoxia

10.6.1.1 In-vitro Experimental Studies

Hohn et al. (1976) showed that bacterial killing of *Staphylococcus aureus* is jeopardized when PO_2 is less than 30 mm Hg. With PO_2 approaching 0 mm Hg bacterial killing is diminished by 50%. The reason for this is that bacterial killing is caused by reactive oxygen species present in neutrophils. These reactive oxygen species are generated from the oxygen contained in surrounding tissues (neutrophils in this stage demonstrate a 30-fold

Table 10.1 Correlation of surgical wound infection with low tissue oxygen pressure (PO2). (From Hopf et al. 1997)

Tissue oxygen tension PO² (mmHg)	40–49	50–59	60–69	70–79	80–89	90–99	100–109	110–119	120–129
Ratio infected cases/ examined cases	6/14	7/25	8/33	4/24	2/19	0/7	0/4	0/2	0/2

increase in oxygen consumption over neutrophils in a resting state). In the case of anoxia, neutrophils will cease producing free oxygen radicals and hence will reduce bacterial killing (Curnute and Babior 1975). Impaired bacterial killing has been found for *P. vulgaris*, *K. pneumoniae*, *S. albus*, *S. tiphimurium*, *P. aeruginosa*, and *E. coli* (Mandel 1974; Niinikoski et al. 1972.). Infection in turn is also extremely oxygen consuming and will aggravate hypoxia with PO_2 values approaching zero (Mathieu and Wattel 2006), allowing anaerobes to grow or initiating a vicious circle of aggravating hypoxia and infection (Selvaraj and Sbarra 1966).

10.6.1.2 In-vivo Experimental Studies

The impairment in leukocyte phagocytic activity has been shown in rat models for *S. aureus*, *E. coli*, *K. pneumoniae*, and *P. aeruginosa* (Chang and Mathes 1982; Gottrup et al. 1983; Harris et al. 1977; MacRipley and Sbarra 1967). Esterhai et al. (1986) and Mader et al. (1980) found that medullar infection in a rabbit tibia with *S. aureus* would provoke a fall in oxygen tension (21 mm Hg). This lowered oxygen tension was insufficient for an adequate phagocytic function of leukocytes. Bacterial killing of phagocytosed bacteria was reduced to 30% compared with uninfected normal bone (45%).

10.6.2 Host Defenses Are Increased by Hyperoxia

10.6.2.1 In-vitro Experimental Studies

According to Allen et al. (1997), the production of oxygen radicals is PO_2 dependent. Neutrophils have an oxidant production in normoxia (PO_2 of 45–80 mm Hg) that can be doubled in hyperoxia (PO_2 over 300 mm Hg). Mader et al. (1980) showed that an increase in PO_2 from 45 to 150 mm Hg was able to increase the bactericidal activity of neutrophils from 44 to 71%.

10.6.2.2 In-vivo Experimental Studies

In the experiment described previously, Esterhai et al. (1986) showed also that HBO was able to correct hypoxia to a level of hyperoxia in the same osteomyelitis model as mentioned above. This led to normalization of the phagocytic function of the leukocytes resulting in better control of the bone infection. Jonsson et al. (1988) showed in a model of infection in fresh musculo-cutaneous flaps that hyperoxia would diminish the size and number of infection with *S. aureus*. Hunt et al. (1975) found that HBO-treated rats have a better bacterial clearance of their *P. aeruginosa*-infected exudates compared with an untreated control group. Knighton et al. (1986) demonstrated similar results with *E. coli* bacteria, showing a superior bacterial clearance with HBO compared with the clearance obtained with penicillin.

10.7 Effect of Hyperbaric Oxygen on Anaerobes

10.7.1 In-vitro Experimental Studies

Oxygen is lethal to most anaerobes because these bacteria lack protection enzymes such as superoxide dismutase or catalase. Normoxia (PO_2=152 mm Hg) kills *P. magnus*, *B. fragilis*, and *C. perfringens* (Walden and Hentges 1975). Oxygen is bacteriostatic to *E. coli* (Muhvich et al. 1989), *Enterobacteriacae*, *P. aeruginosa*, and *E. faecalis* (Park et al. 1992). The effect of oxygen on some important pathogenic anaerobes is shown in Table 10.2.

10.7.2 In-vivo Experimental Studies

Many studies have shown that HBO is bacteriostatic to *C. perfringens* either alone or in combination with antibiotic therapy or surgery (Holland et al. 1975; Demello et al. 1973; Hill and Osterhout 1972). Hyperbaric oxygen

Table 10.2 In-vitro oxygen susceptibility of strictly anaerobic bacteria (Adapted from Loesche 1969)

Bacteria \ Pressure of oxygen (mmHg)	0	1	2	3.5	5	8	15	20	30	45	60	75	90
Clostridium haemolitycum	++	++	++	++	+	0	0						
Peptostreptococcus	++	++	++	++	++	++	+	0	0				
Clostridium novyi	++	++	++	++	++	++	+	0	0				
Bacteroides oralis	++	++	++	++	++	++	++	++	+, V	+, V	0	0	
Prevotella melaninogenica	++	++	++	++	++	++	++	++, V	++, V	+, V	+, V	0	0
Fusobacterium nucleatum	++	++	++	++	++	++	++	++	++	++	+, V	0	0
Bacteroides fragilis	++	++	++	++	++	++	++	++	++	++	+, V	0	0

++ : Normal development
\+ : Reduced development
V : Development according to strain or incubation duration
0 : No development

has also been shown efficient in hepatic abscesses due to *B. fragilis* (Hill 1976) as well as in multibacterial peritonitis with *E. coli*, *Enterococci* and *B. fragilis* (Thom et al. 1986). In such instances, as well as for *Clostridium* infections a combined "clinical approach," in experimental rat peritonitis, combining antibiotics, surgery, and HBO showed the best results (Muhvich et al. 1988).

10.8 Effect of Hyperoxia on Aerobes

10.8.1 In-vitro Experimental Studies

Hyperbaric oxygen has no direct bactericidal effect on aerobic bacteria. Hyperbaric oxygen is only bactericidal for aero-anaerobic bacteria such as *S. aureus* or *E. coli* at pressures and duration of exposure which are lethal for humans.

10.8.2 In-vivo Experimental Studies

When PO_2 is 30 mm Hg, bacterial killing is increased by 20% compared with a partial pressure of 1–2 mm Hg. When PO_2 reaches 150 mm Hg, bacterial killing increases another 10% (Hohn et al. 1976). Hamblen et al. (1968) and Mader et al. (1978) showed a positive effect of hyperbaric oxygen on a *S. aureus* model of rat osteomyelitis.

Triplett et al. (1982) tested the effect of HBO alone in a model of mandibular osteomyelitis. In this study, osteomyelitis was created in surgically fractured rabbit mandibles by inoculation of *Bacteroides melaninogenicus*. Although HBO did not fully eliminate the infection on histological examination, sinus tract healing and osseous repair were improved, fracture mobility was decreased compared with the control group treated with ambient air.

Numerous animal studies have proved that the bacterial load of wound exudates is increased at low PO_2 and decreased at high PO_2 (Knighton et al. 1986). When *E. coli* is injected in the skin of healthy rabbits, bacteria will disappear in 5 days from the exudates if they breathe 40–45% oxygen, and if the rabbits breathe 12–14% oxygen, bacteria will not clear and the wound infection will become chronic (Hunt et al. 1975). Oxygen can be considered like any bactericidal drug, since its effect on bacterial clearance from infection is dose dependent (Knighton et al. 1990).

10.9 Bacterial Resistance in Surgical Wounds: General Considerations

According to the review on the subject performed by Giamarellou (2000), anaerobes such as *B. fragilis*, which are very susceptible to oxygen, increasingly produce β-lactamases. *B. fragilis* resistance rates to clin-

damycin can approach 25% in certain countries. New antibiotics cannot be really assessed because they are not tested in critically ill patients but only in acute appendicitis, a disease which ends, by definition, with a cure rate over 90% (Giamarellou 2000). Saini et al. (2004), who investigated 131 surgical wounds, found an average of up to 2.3 bacteria per wound, always with anaerobes. Common organisms were *E. coli*, *S. aureus*, *Klebsiella* spp., *P. aeruginosa*, *B. fragilis*, and *Peptostreptococcus* spp. The greatest degree of multidrug resistance to all antibiotics was found in *P. aeruginosa* (52.9%), *Klebsiella* spp., (33.3%), *Proteus* spp. (33.3%), *E. coli* (22.2%), and *S. aureus* (12.5%). In their conclusions, the authors recommend HBO as an adjunct to antibiotics and debridement in the management of surgical infections.

10.10 Effect of Hyperbaric Oxygen on Antibiotics

Recently, Mendel et al. (1999, 2004) showed that HBO added to oral cephalosporins or gentamycin sponges had an additive effect in a rat model of chronic tibial osteomyelitis with *S. aureus*. Hyperbaric oxygen alone led to a significant improvement of the infection; furthermore, the quantitative bacterial count was significantly lowest when HBO was adequately combined with antibiotics. Mader et al. (1978) conducted a similar experiment. They found that HBO alone was as effective as cephalothin to control infection in *S. aureus*-induced chronic osteomyelitis of the tibia in rat. They concluded that HBO has its own bactericidal effect which is not related to direct antibacterial mechanisms. On the contrary, Davey et al. (1987) observed that aminoglycosides, ciproxin, and imipenem lost their microbicidal capacity in hypoxia. Adams et al. (1987) found that HBO would increase the effects of certain aminoglycosides such as tobramycin in a *P. aeruginosa* model. Luongo et al. (1999) confirmed these findings. They found HBO as efficient as amikacin in a rat model of subcutaneous or pulmonary infection with *P. aeruginosa*. They found also a synergistic effect between amikacin and HBO. Results of this study are shown in Tables 10.3 and 10.4.

Park et al. (1991) found that HBO would increase the postantibiotic effect of aminoglycosides on three different strains of *P. aeruginosa*. It appears that HBO is of use in infections with *P. aeruginosa*, a bacteria showing increasing resistance to common antibiotics.

10.11 Effect of Hyperbaric Oxygen on Healing in Difficult Wounds

10.11.1 Experimental Data

Quirina and Viidik (1996) showed that wound healing of normal incision wounds is diminished in old age. Ischemia aggravates further wound healing, whereas HBO is able to improve wound strength up to 50%. Actually, it is thought that reactive oxygen species act as a signal transducer to overexpress growth factor production and growth factor receptors (Tandara and Mustoe 2004).

10.11.2 Clinical Data: Chronic Wounds

Hyperbaric oxygen has been found useful as adjunct in the treatment of chronic refractory osteomyelitis of the tibia when at least 30 sessions were applied (Bilbault et al. 2004; Chen et al. 2004; Davis et al. 1986). Hyperbaric oxygen was also found useful in the treatment of chronic non-healing wounds in diabetic patients (Kessler et al. 2003; Faglia et al. 1996; Abidia et al. 2003), and it was further found to speed healing of chronic venous ulcers (Hammarlund and Sundberg 1994) and chronic radiation wounds. In chronic radiation wounds, it is estimated that pre- and postoperative use of HBO will prevent a postoperative wound dehiscence in every fifth surgical patient. In already existing chronic radiation wounds, it is expected that HBO will close the wound of every fourth patient (Bennet et al. 2005). Marx (1999) describes the positive effect of HBO on the outcome of vascular flaps elevated in irradiated tissue; however the author emphasizes that at least 30 treatments must be applied before surgery to achieve these results (Table 10.5).

10.12 Osteomyelitis of the Jaws: Bacteriological Assessment

10.12.1 Infections in the Immunocompetent Host

Calhoun et al. (1988) found mostly a polymicrobial flora in 60 patients with mandibular bone infection. Anaerobes played an important role in their series. Hudson (1993) made a review of the literature over 50 years and concluded that infections mostly originated from the odontogenic flora. This point of view is shared by Takai

Table 10.3 Effect of HBO and amikacin on bacterial clearance in an experimental infection model with *P. aeruginosa* in a rat model (From Luongo et al. 1999)

Subcutaneous infection	Blood culture		Biopsy tissues		
	n	*P. aeruginosa* at day 8 (%)	*n*	*P. aeruginosa* at day 8 (%)	CFU mg^{-1} of tissue
Control *n*=9	9	100	9	100	10^8
Amikacin *n*=9	2	22.2	2	22.2	10^8
Hyperbaric oxygen *n*=10	1	10	1	10	–
Hyperbaric oxygen + amikacin *n*=10	0	0	0	0	–

Table 10.4 Effect of HBO and amikacin on mortality after experimental subcutaneous or pulmonary inoculation of *P. aeruginosa* in rat model (From Luongo et al. 1999)

Groups	Mortality according to route of infection				
	Subcutaneous		Pulmonary		
	n	%	*n*	%	Day of death
Control *n*=10	1	10	8	80	2.4±0.6
Amikacin *n*=10	1	10	2	22.2	2
HBO *n*=10	0	0	1	10	2
Hyperbaric oxygen + amikacin *n*=10	0	0	0	0	–

Table 10.5 Effect of HBO on outcome of vascular flaps elevated in irradiated tissue (From Marx 1999)

		n	Minor	Major	Total
Wound infections	Non-HBO	80	6(7.5)	13(16)	19(24)
	HBO	80	3(3.5)	2(2.5)	6(6)
Wound dehiscence	Non-HBO	80	12(15)	26(33)	38(48)
	HBO	80	6(7.5)	3(3.5)	9(11)
Delayed wound healing	Non-HBO	80			44(55)
	HBO	80			9(11)

Numbers in paranthesis are percentages

et al. (2005). They found that surgical incisions made during procedures such as decortication for osteomyelitis or tooth extraction would provoke a bacteremia, especially in patients with acute osteomyelitis and periodontitis. In their study, they found mostly *S. viridans*. Chen et al. (2002) also found a vast majority of anaerobes in their study on periodontitis. Giamarellou (2000) shares this opinion in her review article. According to the author many infections, such as dental infections (pulpitis, gingivitis, periapical respiratory or dental abscess, perimandibular space tract infection), chronic sinusitis, recurrent tonsillitis, chronic otitis media, mastoiditis, and peritonsillar abscess are often caused by anaerobes.

10.12.2 Infections in Hosts with Impaired Immune Defenses

There are only anecdotal reports in the literature which deal with this subject. It seems, however, that the frequency of infections with fungi, such as *Zygomycosis* (John et al. 2005), *Mucormycosis* (Guevara et al. 2004), *Actinomyces* spp. (Happonen et al. 1983), *Saccharomyces* spp. (Hovi et al. 1996), *Aspergillus* spp. (Lo et al. 2003), and anaerobes like *Pseudomonas* spp, especially in old diabetic patients (Singh et al. 2005), is increasing.

10.13 Indications for Hyperbaric Oxygen in Craniofacial Infections

As seen in Chap. 8 and 9 the optimal treatment of jawbone osteomyelitis with or without soft tissue involvement is a combination of surgery, antibiotics, and proper wound care. Unfortunately, when bacteria are resistant to antibiotics or when the host defenses are jeopardized by a systemic condition, such as cancer treatment, diabetes, HIV, old age, etc., or when the local vascularization is insufficient, necrosis or relapses are possible. Furthermore, a reduced general medical condition of the patient suffering from osteomyelitis of the jaw may not allow an extensive surgical debridement, which may be required.

Because of the quality of in-vitro and in-vivo evidence, HBO has been used as an adjunct to surgery and antibiotics by many clinicians. They have reported improvement or success when HBO was added to a difficult or desperate clinical situation. Due to the high variability of patients, infectious agents and antibiotic resistance, like for many other treatment modalities, randomized studies are lacking for HBO. We therefore present the existing literature as well as our own experience with this subject.

10.13.1 Soft Tissue Infections

In a retrospective study, Sugihara et al. (2004) compared the duration of treatment in two groups of patients with soft tissue infections in various locations, including the face. The examined patients in this study were all immunocompetent. The authors found a reduced treatment time in the group receiving HBO, attributing this effect to an antibiotic enhancement provoked by HBO. Edwards et al. (2004) report on a patient with fulminant craniocervical necrotizing fasciitis from odontogenic origin. He improved rapidly under a multidisciplinary treatment including appropriate HBO. Stenberg et al. (2004) had the same experience treating 13 cases of cervical necrotizing fasciitis. They confirmed the odontogenic origin of bacteria, mostly *Streptococcus milleri*. Most were intensive care patients needing inotropic drugs, and all recovered with a comprehensive treatment including HBO. Wilkinson and Doolette (2004) reviewed 44 patients treated at a major tertiary hospital for necrotizing soft tissue infection. In that series, the strongest association with survival was associated with the use of HBO. Whitesides et al. (2000) treated another 12 patients with necrotizing fascitis from ondotogenic origin. Treatment protocols included HBO from the beginning. The authors concluded that early surgical intervention and the use of HBO improves clinical outcome.

10.13.2 Osteomyelitis of the Neurocranium and the Orbit

There is sparse literature on this subject. Singh et al. (2005) reported 3 cases secondary chronic osteomyelitis due to *P. aeruginosa* infection in diabetic patients. Two of the described cases were treated without HBO and died, one case healed once HBO was introduced in the multidisciplinary treatment. Larsson et al. (2002) found HBO efficient to salvage skull-bone flaps and acrylic cranioplasties, mostly without removal of fixation systems. This effect was particularly useful in patients with impaired immunological defenses. Follow-up was at least 6 months in all examined patients in that study. Fielden et al. (2002) were able to salvage a worsening patient with clostridial gangrene of the orbit by use of HBO in their therapy.

10.13.3 Osteomyelitis of the Jaws

The purpose of HBO in chronic refractory osteomyelitis of the jaws, whether primary or secondary chronic, is the same as mentioned previously. It reverses the hypoxic state of the infected bone and enhances leukocyte killing of microorganisms, as well as the aforementioned survival and toxin production of certain anaerobes and facultative anaerobes (Marx 1991). As early as 1973, Mainous et al. (1973) reported on treatment of one case of acute osteomyelitis and two cases of secondary chronic osteomyelitis with surgery, antibiotics, and adjunctive HBO. The authors observed a favorable response with a shortened healing period and improved outcome. They concluded that HBO should have a definite place in osteomyelitis of the mandible. Aitasalo et al. (1998) treated 33 consecutive patients with chronic osteomyelitis of the jaw. According to the classification advocated in this book, the cases were mostly secondary chronic; however, cases of osteoradionecrosis were also included in the study. The median follow-up time was 34 months. The patients had five to ten preoperative and five to seven postoperative sessions. Surgical therapy consisted of decortication of the affected bone, subsequently covered with a free periosteal transplant from the tibia. Twenty-six patients (79%) with chronic osteomyelitis have remained symptom-free after the first treatment period. The seven failed osteomyelitis patients needed retreatment, and five of them still had occasional clinical symptoms at the end of the follow-up period. The authors concluded that HBO is a useful adjunct therapy for (secondary) chronic osteomyelitis of the jaws; however, the effectiveness of the low number of HBO treatment sessions used, which was reduced compared with earlier protocols, must be questioned. Van Merkesteyn et al. (1984) also used HBO as an adjunct to surgery and antibiotics for the treatment of secondary chronic osteomyelitis of the jaws. They found HBO to be a useful adjunct in cases of chronic diffuse sclerosing osteomyelitis (according to the classification used in this book, these cases are mostly classified as secondary chronic osteomyelitis, in some instances as primary chronic osteomyelitis) and in cases where decortication and antibiotics had failed. Jamil et al. (2000) treated 16 patients with therapy resistant (secondary) chronic osteomyelitis of the mandible with 30 adjunctive HBO sessions. Six patients were healed and 8 improved. Baltensperger et al. (2001) made a retrospective study of patients treated for acute and secondary chronic osteomyelitis of the jaws. Only patients who received at least 20 sessions of HBO were included. Forty-three patients were identified and compared with a randomly chosen control group treated at the same time and at the same institution treated without adjunctive HBO. Follow-up was 1.62 years (0.25–9 years). Both groups were comparable with the exception that there were significantly more patients with a history of alcoholism and cigarette smoking in the HBO group. All patients received clindamycin 3×300 mg/day or cefuroxime 2×500 mg/

Table 10.6 Multidisciplinary treatment of osteomyelitis of the jaw: clinical symptoms at end of follow-up (From Baltensperger et. al 2001)

	With HBO	Without HBO
No symptoms	28	31
Less symptoms	10	8
Unchanged symptoms	5	4
Worsening of symptoms	0	0

Table 10.7 Multidisciplinary treatment of osteomyelitis of the jaw: surgical procedures at end of follow-up (From Baltensperger et. al 2001)

Major surgery	28	36
Minor surgery	12	5
No surgery	3	2

day for 2 weeks as a standard. The results of this study are presented in Tables 10.6 and 10.7.

There was no statistical difference in clinical outcome between both groups. The importance of smoking and alcoholism on outcome could not be evaluated; however, adjunctive HBO seemed to reduce the amount of major surgical procedures such as decortication and resection, without jeopardizing the outcome. Practically, Baltensperger et al. (2001) concluded that adjunctive HBO and antibiotics may allow a more limited surgery in patients with localized osteomyelitis of the jaw. Although the number of patients of that study was small, the authors felt that HBO was most efficient when sessions were applied pre- and post-operatively.

Handschell et al. (2007) examined the outcome of 27 patients with mostly secondary chronic osteomyelitis that had been treated with HBO. The authors concluded that adjuvant HBO therapy was successful in the treatment of patients with chronic osteomyelitis which could avoid ablative surgery in some instances.

According to Undersea and Hyperbaric Medical Society, the use of HBO as an adjunct therapeutic tool is indicated for refractory osteomyelitis; however, despite the positive experiences which several authors have described in using HBO for treatment of osteomyelitis of the jaws, the literature on this topic is scarce compared with other used therapeutic modalities. No study has yet provided actual statistical data on the actual benefits of HBO on the outcome of patients. Prospective randomized multicenter studies do not exist. The studies mentioned above mostly described the use of HBO for cases of secondary chronic osteomyelitis. In cases of primary chronic osteomyelitis the use of this therapeutic regime is even more controversial and in some instances anecdotal, since most reported experiences are case reports. Personal experiences of the editors of this book indicate that HBO may alleviate symptoms and help avoid extensive surgery in cases of early-onset primary chronic osteomyelitis.

10.13.4 Refractory Craniofacial Mycoses

There is only very limited experience on this subject. Most case reports published are summarized in Table 10.8. Patients in mentioned studies were usually directly treated with HBO.

John et al. (2005) made a review of 28 cases with zygomycosis. They found a survival rate approaching 94% in diabetic patients. Prolonged HBO therapy was associated with 100% survival. Hyperbaric oxygen seemed, in contrast, doubtfully active in patients with hematological malignancies with only 33% survival.

10.14 Conclusion

It is well known that infection is oxygen consuming and leads to local hypoxia, which in return favors the spread of infection. Hyperbaric oxygen can correct this

Table 10.8 Outcome of zygomycosis

Reference	Agent	*n*	Course before HBO	HBO	Death
Marzo and Leonetti (2003)	?	4	–	–	3
Garcia-Covarrubias et al. (2002)	Mucormycosis	5	HBO from Start	+	2
Chassaing et al. (2003)	Mucormycosis	1	Worsening	+	0
Garcia-Covarrubias et al. (2004)	Aspergillosis	6	HBO from Start	+	3
Pelton et al. (2001)	Mucormycosis	1	HBO from Start	+	1
Guevara (2004)	Mucormycosis	9	HBO from Start	+	5
Simmons et al. (2005)	Mucormycosis	1	HBO from Start	+	0

situation. In oral infections, anaerobes are mostly involved in immunocompetent hosts, while opportunistic infections play a major role in hosts with impaired immune defenses. There is a large and sound body of experimental in-vivo and in-vitro evidence showing that:

- Hyperbaric oxygen is directly bactericidal or bacteriostatic to anaerobes.
- Hyperbaric oxygen is efficient for bacterial control in infections with most type of aerobes, mainly through a direct host effect by improvement of the killing mechanism of neutrophil granulocytes.
- Hyperbaric oxygen can restore the bactericidal effect of aminoglycosides. It shows at least an additive effect to cephalosporines.

There is limited evidence demonstrating that:

- Hyperbaric oxygen improves wound healing experimentally and clinically in chronic nonhealing wounds.
- Hyperbaric oxygen as an adjunct to standard care has been showed to be associated with better healing and improved survival in patients with cervical necrotizing soft tissue infections.
- Hyperbaric oxygen as an adjunct to standard care has been suggested to allow better infection control in severe infections involving osteomyelitis of the neurocranium and the orbit.
- Hyperbaric oxygen as an adjunct to standard care has been associated with a reduced need for major surgery in acute and secondary chronic osteomyelitis of the jaws.
- Hyperbaric oxygen associated to standard care has been showed to improve survival and infection control in zygomycosis, especially in diabetic patients.

Hyperbaric oxygen has the potential to be a very useful adjunct in the treatment of infections in head and neck surgery; however, carefully designed trials, avoiding methodological bias due to the great variability of patients, infectious agents, antibiotic resistance, host factors, etc., are still lacking and are needed to broaden the evidence of this therapeutic modality.

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Osteomyelitis of the Temporomandibular Joint

11

Michael Kaufmann and Joachim Obwegeser

Contents

11.1 Summary

Osteomyelitis of the temporomandibular joint (TMJ) is a rare condition. Epidemiology, pathogenesis, clinical signs, and complications are presented with review of the scarce literature on this topic and our personal data. Due to the complexity of the TMJ, therapy is challenging even for the experienced clinician. As with osteomyelitis in other parts of the jawbone, surgery is one of the major pillars of therapy for bone infections in this location. Since advanced cases of osteomyelitis involving the TMJ usually demand surgical resection of the condyle, special emphasis is given this topic in the second part of this chapter, including discussion of different reconstructive procedures of the TMJ. The experience of the authors is outlined in a description of there protocol in handling of TMJ osteomyelitis.

11.2 Introduction

Osteomyelitis of the temporomandibular joint (TMJ) is a very rare condition and mostly occurs together with osteomyelitis in other locations of the mandible as a result of local spreading of the bone infection.

Solitary osteomyelitis in the TMJ without involvement of other parts of the jawbones is even more seldom and only scarce case reports exist (Kaufmann et al. 2005). Herein an overview of this rare location of osteomyelitis is presented with focus on possible treatment strategies in modern maxillofacial surgical practice.

11.3 Epidemiology

Epidemiological data about involvement of the TMJ in osteomyelitis are difficult to obtain because most studies dealing with osteomyelitis of the jaws do not mention the mandibular condyle separately. In a retrospective study by Calhoun et al. (1988) the TMJ was involved in 2% of totally 60 examined patients with secondary chronic osteomyelitis (SCO); however, they included 28 patients with osteoradionecrosis. In a retrospective study of the Department of Cranio-Maxillofacial Surgery at the University Hospital Zurich in the past 30 years (1970–2000)

290 patients with osteomyelitis were retrospectively assessed (Baltensperger 2003). All osteomyelitis cases were classified into three major groups of osteomyelitis: acute osteomyelitis (AO); secondary chronic osteomyelitis (SCO); and primary chronic osteomyelitis (PCO). Cases of osteoradionecrosis were excluded from the study. No patients with acute osteomyelitis (AO) had involvement of the TMJ, whereas 5 patients (2.6%) with secondary chronic osteomyelitis (SCO) showed affection of the mandibular condyle. A plate of cortical bone separating the condylar neck from the ascending ramus with lack of an actual medullar cavity is believed to be responsible for this rarely observed spreading of the infection from the ascending ramus into the mandibular condyle (Winiker-Blanck et al. 1978).

Contrary to these observations in acute and secondary chronic osteomyelitis, Baltensperger (2003) demonstrated an involvement of the condyle in almost 50% (14 of 30 patients) of the assessed cases with primary chronic osteomyelitis. The cause therefore remains unclear as long as the pathogenesis of this diseases entity is not fully understood and, despite being the one of the largest groups of primary chronic osteomyelitis cases found in literature, 30 cases are not sufficient to draw statistically significant conclusions.

11.4 Pathogenesis

11.4.1 Primary Chronic Osteomyelitis of the Temporomandibular Joint

As mentioned above, the pathogenesis of primary chronic osteomyelitis remains unclear. It is a chronic, nonsuppurative disease that almost exclusively affects the mandible. Several possible mechanisms are discussed in the literature. One common theory is an exaggerated immune response triggered by a low-grade infection (Eyrich et al. 1999). A dental born infection seems to be unlikely, since primary chronic osteomyelitis was also observed in edentulous individuals as well as in patients lacking a dental focus (Baltensperger 2003). Groot et al. (1992a,b) postulate that diffuse sclerosing osteomyelitis, a term that is mostly used interchangeably with primary chronic osteomyelitis, may be a reactive hyperplasia of bone resulting from chronic tendoperiostitis, initiated and exacerbated by chronic overuse of the masticatory muscles. In the studied patient collective from the Department of Craniomaxillofacial Surgery in Zurich, 37% of the patients with diagnosed primary chronic osteomyelitis demonstrated TMJ pain in the medical history (Baltensperger 2003). In some cases the symptoms were initially misinterpreted as myofacial pain syndrome. The fact that almost two thirds of the patients did not show any myofacial and/or TMJ pain symptoms does not support the hypotheses of Groot and coworkers (1992a,b).

11.4.2 Acute and Secondary Chronic Osteomyelitis of the Temporomandibular Joint

The presumed etiology and pathogenesis of acute and secondary chronic osteomyelitis of the TMJ does not differ from other cases of suppurative osteomyelitis of the jawbone which are discussed extensively in Chap. 2. The TMJ is mostly infected *per continuitatem* from an infected mandibular angle and ascending ramus.

The presentation of solitary osteomyelitis of the TMJ, however, can have further causes such as suppurative (septic) arthritis, malignant external otitis, and iatrogenic local inoculation of microorganisms:

Suppurative septic arthritis concerns almost exclusively adults and is a very rare disease (Leighty et al. 1993). Infections of the middle ear, mastoid, and parotid gland can spread to the TMJ. Superinfected open joint fractures of the condyle, infections caused by diagnostic joint aspirations or hematogenous spread of infections from other locations could be further reasons. In the past syphilis, tuberculosis, gonorrhoea, and scarlet fever were described to cause joint infection (Wurman et al. 1979). Once bacteria gain access to the synovial space, they can cause irreversible changes within a few days (Leighty et al. 1993). Osteomyelitis, fibrous or bony ankylosis, and disturbances of growth can succeed.

In rare cases malignant external otitis can spread to the TMJ and establish an osteomyelitis (Drew et al. 1993; Calhoun et al. 1988; Midwinter et al. 1999). In these instances the infection is frequently caused by *Pseudomonas aeruginosa* and usually occurs in patients with impaired immunological defense mechanisms. Typically, elder people with diabetes mellitus are affected. If not treated early, this disease may be fatal; hence, the term malignant.

Iatrogenic inoculation of bacteria by use of local anesthetics for dental treatment is discussed in some instances; however, it has not been proved (Kaufmann et al. 2005).

11.5 Clinical Findings and Diagnosis

Most, but not all, patients with osteomyelitis of the TMJ present with myofacial pain. Further signs are swelling of the preauricular region, reduced mouth opening caused by inflammation of the TMJ and/or inflammation of the masticatory muscles (Fig. 11.1a,b), and derangements of occlusion. Furthermore, abscess and fistula formation can occur.

The principles of diagnostic imaging are no different than in osteomyelitis cases involving other parts of the jaws and hence can also be applied in the radiological work-up of cases with involvement of the TMJ. In addition to conventional imaging with orthopantomography as a primary scan, computed tomography (CT) is considered the imaging procedure of choice. For follow-up documentations with special questions, e.g., extent of inflammatory edema in bone marrow and the surrounding tissues, magnetic resonance imaging (MRI) could become more and more important. Histological examinations are mandatory to confirm the diagnosis and exclude other pathologies. In cases of mandibular osteomyelitis with involvement of the TMJ histological probes are best taken from the involved area with easiest access.

In cases which are suspicious for solitary osteomyelitis of the TMJ, the possibility of a primary or metastatic malignancy must be excluded by histological confirmation (Kanemoto 1992).

11.6 Complications

Similar to secondary chronic osteomyelitis involving other parts of the jaw, abscess and fistula formation also occur when the infection affects the TMJ and the peri-



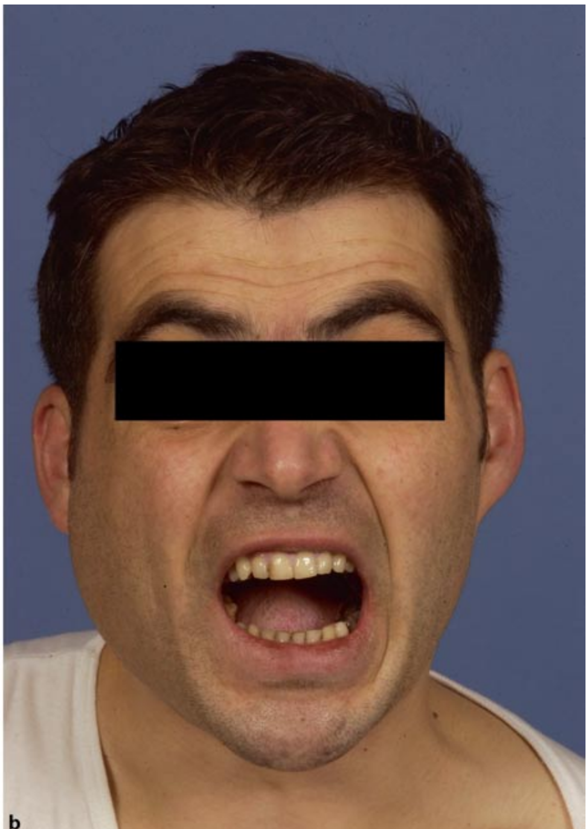


Fig. 11.1a,b A 25-year-old man with a secondary chronic osteomyelitis (SCO) of the right mandibular angle and condyle: Initial clinical presentation with diffuse perimandibular and preauricular swelling combined with trismus is observed. (This case is described in detail in Chap. 12, case report 8)

articular soft tissue (Fig. 11.2). These symptoms eventually demand for surgical intervention. Destruction of the articular surfaces can eventually result in fibrous or bony ankylosis with permanent derangements of the occlusion.

A very rare complication of primary chronic osteomyelitis associated with SAPHO syndrome with involvement of the TMJ has been described to cause sudden deafness (Marsot-Dupuch et al. 1999).

11.7 Therapy

When the TMJ is affected in primary or secondary chronic osteomyelitis, the following three decisions have to be made:

1. Conservative or surgical therapy (e.g., resection of the condyle)
2. Immediate or secondary reconstruction of the TMJ after surgical resection
3. Alloplastic or autogenous joint replacement

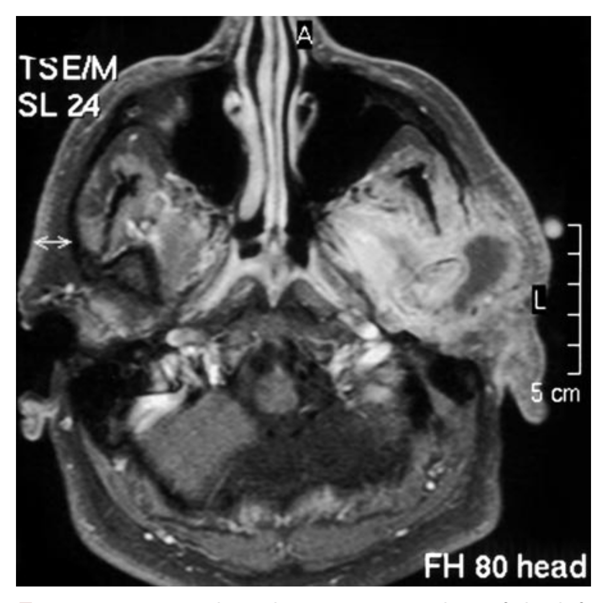


Fig. 11.2 Secondary chronic osteomyelitis of the left temporomandibular joint: Axial MRI scan demonstrates an abscess in the left preauricular region (hypointense area) surrounded by diffuse tissue infiltration (hyperintense area) involving the left lateral pterygoid muscle. (This case is described in detail in Chap. 12, case report 12)

11.7.1 Conservative vs. Surgical Therapy

In cases of primary and secondary chronic osteomyelitis involving the TMJ the principles of therapy are basically the same as in osteomyelitis involving other regions of the jaw. These principles are discussed in detail in Chap. 8. If surgical therapy is considered an option, resection of the condyle is mostly the procedure of choice in advanced cases, because it is the most efficient or in most cases the only way to ensure a complete debridement of infected bone tissue; however, if possible, a more conservative surgical approach should always be considered an option.

It is well accepted that surgical treatment of primary chronic osteomyelitis shows variable success. Furthermore, the effects are only short-termed in most instances. Decortication and removal of necrotic tissue may be useful in early (active) stages of the disease; however, due to the uncertain prognosis, excessive ablative surgery should be avoided, especially in young patients. Records from patients with primary chronic osteomyelitis from 1970 to 2000 treated at the clinic of Cranio-Maxillofacial Surgery of the University Hospital Zurich presented involvement of the TMJ in 11 of 30 cases (Baltensperger 2003; Baltensperger et al. 2004). Only one of these patients underwent condylar resection.

Long-term antibiotics, hyperbaric oxygen therapy, nonsteroidal anti-inflammatory drugs, corticosteroids, and recently sodium clodronate have been reported as beneficial for treatment; however, no studies of larger patient groups have been conducted thus far to provide confirmation (Baltensperger 2003).

Surgery has always been a major column of therapy in acute and especially secondary chronic osteomyelitis therapy. Baltensperger (2003) found a total of 5 patients of 203 (2.6%) patients with secondary chronic osteomyelitis involving the condyle/temporomandibular joint. In all of these cases local debridement was preferred over total resection of the condyle due to the low extent of the infection.

In the few cases of a solitary secondary chronic osteomyelitis affecting the TMJ, debridement or resection of the condyle were performed (Kaufmann et al. 2005).

11.7.2 Immediate or Secondary Reconstruction of the Temporomandibular Joint After Resection

The therapy of choice was condylar resection in the majority of solitary secondary chronic osteomyelitis cases

affecting the TMJ described in the literature; however, in none of the cases reported was an effort for simultaneous reconstruction undertaken. Obwegeser (1960) proposed an active surgical approach in cases of jawbone osteomyelitis in 1960, emphasizing the necessity for a sufficient debridement of the affected bone. He described a primary reconstruction of the TMJ and ascending ramus with iliac crest after resection in a case of secondary chronic osteomyelitis.

Recent experiences have encouraged the authors to favor immediate reconstruction of the TMJ in the same procedure, even in infectious cases. Despite the fact that simultaneous reconstruction in these instances does harbor a significant risk for infection of the inserted implant or transplant, this protocol does have the advantage of immediate reconstruction of anatomical dimensions which facilitates possible further reconstructions. If condylar resection is performed without (temporary) compensation of the created dead space with a placeholder (e.g., condylar prosthesis), the forces of the scar tissue will inevitably destroy the posterior vertical height and hence create an open-bite situation. This sets a very difficult precondition for further definite reconstructive procedures.

11.7.3 Reconstruction Modalities

The rare appearance of osteomyelitis affecting the TMJ hinders large experience for specific reconstructive procedures. In the retrospectively analyzed 290 cases of osteomyelitis, Baltensperger (2003) found only one reconstruction of the condyle performed, which was achieved by using an autogenous costochondral graft. Nevertheless, two recently treated patients by the authors with secondary chronic osteomyelitis involving the condyle had to be reconstructed with simultaneous placement of prosthesis as a placeholder. Experiences of these cases and a review of data gathered from the literature are included in the following overview of the different reconstruction methods.

In modern reconstructive surgery of the TMJ many different solutions exist. Like any medical procedure where a variety of modalities are proclaimed, there appears to be no perfect single solution; hence, every suggestion must be questioned regarding all advantages and disadvantages.

Two main reconstruction modalities of the TMJ exist: autogenous and alloplastic. Up to now the most suitable method of reconstruction remains a controversial issue in the literature.

11.7.3.1 Autogenous Reconstruction

11.7.3.1.1 Free Grafts

Several autogenous tissues have been used for free replacement grafting of the mandibular condyle in the past: iliac bone; clavicle and sterno-clavicular joint; fibular head; metatarsal bone; metatarsophalangeal joint; and costochondral graft (Lindqvist et al. 1986). The worldwide most accepted technique is the costochondral graft. Sir Harold Gilles described this procedure in 1920’s. Since then it has been used numerously in reconstructive procedures with a vast amount of data published. The advantages of the costochondral graft are (Perrott et al. 1994; Saeed and Kent 2003):

1. Biological compatibility, without the possibility of foreign-body reaction
2. Similarity to the condylar anatomy
3. Functional adaptability of the tissue allowing a certain degree of remodeling
4. Growth potential
5. Minimal donor-site morbidity

An important aspect of the use of costochondral grafts in children is the growth potential of these grafts (Figueroa 1984); therefore, this type of surgery is considered the preferred method in treating ankylosis of the TMJ in these young patients. While some authors do not see any problems with linear overgrowth of the graft, others observed massive mandibular prognathism after bilateral joint replacement with a costochondral graft. The thickness of the transplanted cartilage cap seems to be of importance (Ko et al. 1999; Peltomäki et al. 1992; Perrott et al. 1994).

The major disadvantages of the costochondral graft are (1) unpredictable growth with potential overgrowth, and (2) the possibility of reankylosis when used for treatment of ankylosis.

Further possible complications are fracture, donor-site morbidity (e.g., pneumothorax), and insufficient vascularization with consecutive loss of the graft due to scar tissue often found in multiple-operated patients (Mercuri 2000). Furthermore, giant cell reactions caused by wear debris of previous alloplastic materials or inflammatory diseases affecting the TMJ can harm free autogenous grafts (Wolford 1997).

11.7.3.1.2 Vascularized Grafts

The free vascularized metatarsal and free fibula microvascular flap are examples of commonly used vascularized grafts for replacement of the mandibular condyle (Bond et al. 2004; Wax et al. 2000). Due to its dimensions, with a maximal length up to 7 cm, the metatarsal bone offers adequate tissue be used for exclusive reconstruction of the mandibular condyle; however, in larger resections the amount of offered tissue is insufficient. In contrast to the free fibular graft, the metatarsal head provides an articular surface with cartilage and even an epiphyseal growth plate which allows further growth in childhood. The main disadvantage is the loss of a toe. Because of its larger amount of bone, a free fibular graft will instead be chosen to reconstruct more extended parts of the mandible including the condyle. Up to now, both methods have limited indications and are not commonly the first choice of reconstruction of the TMJ.

11.7.3.2 Alloplastic Reconstructions

Basically, one can distinguish between three major types of TMJ prosthesis: (1) the TMJ fossa-eminence prosthesis; (2) the TMJ condylar prosthesis; and (3) the TMJ total-joint prosthesis (van Loon et al. 1995). The most commonly used types are the condylar and the total-joint prosthesis, which are discussed briefly. A more extensive description of alloplastic reconstruction of the TMJ is presented in several other books and is beyond the scope of this one.

11.7.3.3 Condylar Prosthesis

Condylar prosthesis is fixed by a metal plate screwed to the mandible. By varying the extent of the plate it can be used either for single condylar replacement or combined with a more complex reconstruction of the mandible due to more extended resections. The temporary 3D adjustable condylar prosthesis, System Stryker Leibinger (Stryker Leibinger, Freiburg, Germany), and the MODUS temporary condylar prosthesis (Medartis, Basel, Switzerland; Fig. 11.3a,b), are mentioned as examples.

A major problem of these prostheses is that the attrition of the metallic component against the articular cartilage can cause cartilage wear and bone resorption leading to perforation of the fossa roof with exposure of the middle cranial fossa (MacIntosh et al. 2000; Mercuri 2000; van Loon et al. 1995). The fact that the articular disc is removed in most cases of condylar prosthesis implantation additionally increases the risk of bone resorption; therefore, condylar prostheses usually should be used as a temporary replacement only, after resection of the condyle. Condylar prostheses are most useful in maintaining the vertical dimension and the articular function when primary reconstruction is not intended or possible (e.g., because of persistent infection).

11.7.3.4 Total Temporomandibular Joint Prosthesis

The first total TMJ prostheses were developed in the 1960s. In the past four decades three problems have played a consistent and decisive role: (1) wear resistance





Fig. 11.3a,b Two variations of the MODUS temporary condylar prosthesis (Medartis, Basel, Switzerland): Singular condylar replacement device (**a**), condylar prosthesis fixed to a 2.5-mm reconstruction plate which allows more extended reconstructions (**b**)

and wear debris; (2) fitting of the prosthesis; and (3) function of the prostheses.

11.7.3.4.1 Wear Resistance and Wear Debris

The articular surfaces of previous generations of total TMJ prostheses were manufactured of PMMA or Proplast Teflon. Today, the alloplastic condyle is made of cobalt–chromium–molybdenum (Co–Cr–Mo) alloy. The fossa shows a customized design, either of the same material as the condyle or of ultra high molecular weight polyethylene (UHMWPE). These two materials represent the gold standard of orthopedic joint replacement in terms of wear and structural stability (Wolford et al. 1997). Three types are mentioned as examples, which are all approved by the United States Food and Drug Administration: the Christensen prosthesis (TMJ Implants, Golden, Colo.); the TMJ Concepts Patient-Fitted TMJ Reconstruction Prosthesis (TMJ Concepts, Ventura, Calif.); and the Total Temporomandibular Joint Replacement System (Walter Lorenz Surgical, Jacksonville, Fla.).

Particles of materials, such as Proplast Teflon, Silastic, or PMMA, can penetrate in the adjacent soft tissue and bone, where surgical removal is difficult or impossible. They can cause a foreign body giant cell reaction which further affects the graft and hence leads to increased failure rates. Clinical symptoms are chronic pain and impaired function, and in severe cases even ankylosis of the TMJ.

A significant increase failure is reported with an increasing number of surgical procedures involving the TMJ. The residual inflammatory response after removal of alloplastic material is sometimes more severe than that present while the alloplastic graft was still in position (MacIntosh 2000; Wolford 1997; Wolford et al. 2003). Histological studies of patients who received a TMJ Concepts prosthesis (condyle made of Co–Cr–Mo alloy, fossa made of UHMWPE) and no previous alloplastic implants showed no wear debris (Wolford et al. 2003). Further studies with larger patient collectives have yet to be done to prove statistical significance, but the results of Wolford et al. (2003) are promising.

11.7.3.4.2 Fitting

Insufficient fitting of the prosthesis can lead to micromotions with consecutive bone resorption and hence loss of stability (Mercuri and Anspach 2003). The PMMA used as interface between prosthesis and bone in order to optimize the fitting accuracy can cause the aforementioned problems. The TMJ Concepts system is individually manufactured from a 3D plastic model constructed from CT data; however, this technique also harbors some disadvantages. Metallic parts from previous operations cause scattering on the CT scan and have to be removed first. In case of bony ankylosis the cranial joint has to be adapted to the prosthesis, which is a difficult and extensive surgical procedure (van Loon et al. 1995).

11.7.3.4.3 Function

The TMJ is a diarthrodial joint. It harbors a complex biomechanical function, a sliding hinge, which cannot be found in any other joint of the human skeleton. Due to its unique function, the joint is subject to excursions and stresses, which other joints are not. After placement of a total-joint prosthesis, a loss of transitional movements of the condyle is commonly observed. The same observation can be made after replacement of the condyle with a condylar prosthesis or an autogenous graft. The loss of attachment of the lateral pterygoid muscle is discussed as a possible cause. Other reasons may be scarring of the periarticular tissue due to several previous surgical procedures involving the TMJ that most of the patients usually have undergone (van Loon et al. 1995).

A summary of the advantages and disadvantages of total TMJ prosthesis compared with autogenous grafts is given in Tables 11.1 and 11.2.

11.7.3.4.4 Autogenous or Alloplastic Pathway

A retrospective comparison between autogenous and alloplastic joint reconstruction was implemented by Saeed et al. (2002). Both groups investigated in this study had undergone several previous surgical interventions of their TMJs. The preoperative interventions were not further specified. An improvement of symptoms such as pain, mouth opening, and interference with eating occurred in both groups; however, somewhat more favorable results were noted in the group treated with alloplastic joint prosthesis. Because of the higher incidence of recurrent ankylosis and surgical revisions, particularly in patients having undergone several previous surgical procedures of the TMJ, the authors conclude a preference for alloplastic joint prosthesis in the following indications: (1) in patients with a history of ankylosis; (2) after multiple surgical procedures involving the TMJ; and (3) after having previously received alloplastic joints. These indications are consistent with other au-

Table 11.1 Advantages of total temporomandibular joint prosthesis compared with autogenous grafts (Modified after Saeed et al. 2002; Mercuri and Anspach 2003)

Better reproduction of the joint anatomy
No donor site morbidity
Shorter operation time
Reduction of possibility of reankylosis
Immediate beginning of physical therapy

Table 11.2 Disadvantages of alloplastic prosthesis compared with autogenous grafts (Modified after Saeed et al. 2002; Mercuri and Anspach 2003)

Giant cell foreign body reaction due to wear particles
Problems with long-term stabilitiy (e.g., implant fracture or displacement due to loss of screws)
Expensive implants
Lack of growth which precludes the use in children
Allergies to the material of the prosthesis

thors who describe further indications in chronic inflammatory diseases affecting the TMJ causing condylar destruction such as autoimmune diseases, e.g., chronic polyarthritis or lupus erythematosus (Mercuri and Anspach 2003; Wolford et al. 2003).

Due to the abovementioned disadvantages, mainly the possibility of foreign body reactions and because there is an alternative therapy to alloplastic joint replacement, many other surgeons clearly prefer the autogenous costochondral graft. In patients with a residual alloplastic material or reactive tissue due to wear debris, MacIntosh (2000) recommends an observation period of 12 months after aggressive surgical debridement of the TMJ with no attempt at reconstruction in this time period. Reconstruction is then done after a second surgical exploration with no evidence of residual alloplastic material or reactive tissue.

11.7.4 Osteomyelitis of the Temporomandibular Joint: Personal Therapeutic Strategies

Regarding the abovementioned advantages and disadvantages of the various reconstructions, our experience advocates the following procedure in cases of osteomyelitis involving the TMJ which require surgical therapy:

- Resection of the condyle and immediate reconstruction with temporomandibular condylar prosthesis. Maintenance of the vertical dimension, immediate postoperative function, missing metallic wear debris, shorter operation time compared with other reconstruction modalities, and absence of donor morbidity are the main factors for our preference for temporary primary reconstruction whenever possible.
- After resection, the diagnosis must be confirmed by histological examination as precisely as possible.
- An observation period of at least 12 months after primary resection combined with long-term antibiotics (>3 months) and hyperbaric oxygen therapy (>20 sessions) is mandatory. Clinical, radiological, and immunological absences of any signs of persistent infection are necessary before the second-stage surgery is undertaken.
- A secondary definitive reconstruction should be done within a period of 2 years to avoid resorption of the fossa especially in younger patients. Any method of reconstruction of the TMJ can then be selected and, in the rare cases of osteomyelitis of the TMJ, it will always be an individual decision. We prefer either autogenous costochondral or a microvascular graft with first priority.
- In patients who require a more extensive resection due to advanced osteomyelitis, including the ascending ramus and possibly the angle and mandibular corpus, primary reconstruction of the mandible, including the condyle with a microvascular fibular graft, is our method of choice.

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Case Reports

12

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Michael Kaufmann, Richard Lebeda, Joachim Obwegeser

Contents

12.1 Summary

This last chapter of the textbook encompasses a variety of osteomyelitis cases, covering the full scope this disease. Typical case reports as well as cases with a complex course of osteomyelitis (acute, secondary, and primary chronic) are described and illustrated. Furthermore, the final section of this chapter is dedicated to atypical (borderline) cases of primary chronic osteomyelitis.

12.2 Acute Osteomyelitis: Case Reports

12.2.1 Case Report N° 1

Neonatal, Tooth-germ-associated Acute Osteomyelitis

Case Report N° 1 – Summary	
Diagnosis	Neonatal acute osteomyelitis
Affected bone	Right maxilla
Patient	Newborn male infant
General medical history	Full-term gestation, normal delivery
Dental/maxillofacial-related medical history	–
Clinical symptoms	Swelling of the right eye and medial canthus Purulent discharge/fistula formation in the alveolar crest of the right maxilla
Treatment	Antibiotic therapy Surgical drainage of abscess

A 3-week-old Chinese boy was referred by his general practitioner with a swelling of the right eye and associated purulent nasal discharge and a 2-day history of fever. After full-term gestation, the baby was born by normal delivery and weighed 3340 gm The condition of the baby after birth was good and there were no other postnatal problems.

The general clinical examination was unremarkable, except for a mild septic condition. The baby was irritable and had a temperature of 38.2°C. The medial canthus of the right eye was swollen, with a diffuse inflammation spreading to the lower eyelid (Fig. 12.1a,b). Eye movement was normal and the pupils were of equal size and reacted to light. There was no proptosis, chemosis, or ophthalmoplegia. The baby was started on 150 mg of i.v. ampicillin and cloxacillin at six hourly intervals and 6 mg of gentamicin eight hourly. Nasal swab and blood were taken for culture and sensitivity tests. A lumbar puncture was performed to exclude the possibility of early meningitis.

The microbiological examination revealed colonies of *Staphylococcus aureus*, sensitive to cloxacillin, gentamicin, and erythromycin but resistant to penicillin, ampicillin, neomycin, chloramphenicol, and claforan. The cerebrospinal fluid (CSF) was found to be clear and of normal flow rate. The CSF profile was normal. The intravenous antibiotic was revised to cloxacillin (200 mg every 6 h) with topical application of gentamicin and fusithalmic cream to the affected eye. The baby was then referred to the Department of Otolaryngology and a tentative diagnosis of ethmoiditis was suggested.

The following day, the baby's condition worsened and he was noted to have a yellowish discharge from the mouth. A referral to the Oral and Maxillofacial Department was made. Examination of the mouth revealed a purulent discharge at the alveolar crest of the upper right quadrant. There was also a mid-palatal soft tissue swelling measuring 3×3 mm. The baby's general condition was that of mild to moderate infection. A diagnosis of maxillary osteomyelitis of the neonate was made. Under a general anesthetic an alveolar crest abscess was drained. The mid-palatal swelling was found to be continuous with the alveolar crest abscess. Culture and sensitivity test again confirmed the presence of *Staphylococcus aureus* infection sensitive to cloxacillin. The baby was put on a ventilator for 2 days: 200 mg of intravenous cloxacillin at 6-h intervals was maintained. Comprehensive microbiological and radiological tests were carried out but failed to implicate immunodeficiency as the underlying cause of maxillary osteomyelitis and the etiology remained unknown.

The baby's clinical condition improved remarkably over the following 2 weeks and he was subsequently discharged. At a review appointment 6 months later, there was no recurrence of the disease.



Fig. 12.1a,b Newborn with acute osteomyelitis of the right maxilla. Note the swelling of the right cheek and eye and inflammation of the medial canthus of the newborn infant (From Loh and Ling 1993)

12.2 Acute Osteomyelitis: Case Reports

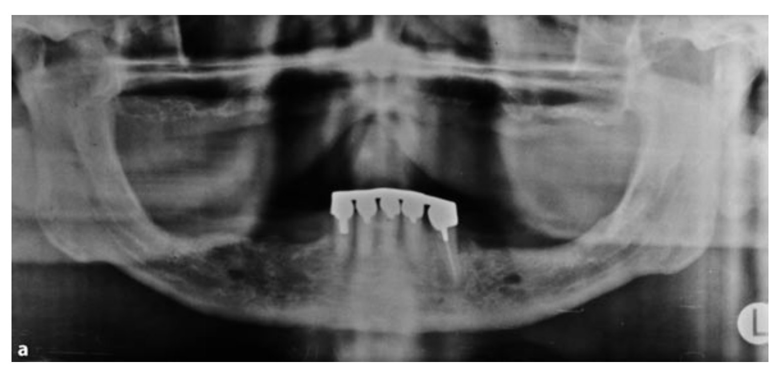
12.2.2 Case Report N° 2

Odontogenic Acute Osteomyelitis

Case Report N° 2 – Summary	
Diagnosis	Odontogenic acute osteomyelitis
Affected bone	Right mandibular corpus
Patient	73-year-old man
General medical history	Uneventful
Dental/maxillofacial-related medical history	For years has chronic periodontal disease in remaining teeth mandible, edentulous maxilla
Clinical symptoms	Acute periodontal abscess formation Pain in lower right anterior mandible with local swelling Hypoesthesia of the mandibular nerve Fistula formation
Treatment	Antibiotic therapy Hyperbaric oxygen

A 73-year-old patient presented with a short history of acute onset of pain in the right lower jaw. The dentist diagnosed an acute periodontal infection with local abscess formation. Incision and drainage of the abscess were performed as well as a local periodontal debridement. Additional per oral antibiotics were administered. No clinical improvement was noted. Follow-up OPG 3 weeks after onset of clinical symptoms demonstrated suspicious rarefaction of spongiosa in the left mandible (Fig. 12.2a). The patient was referred to our clinic for further work-up and treatment. On initial presentation he showed a limited opening of the jaw with local pain and swelling of the right mandible and hypoesthesia of the mandibular nerve. A small fistula with pus was noted in region of the right lower first molar. The CT exams confirmed the suspected diagnosis of an acute odontogenic osteomyelitis (Fig. 12.2b).

Initial treatment consisted of hyperbaric oxygen (HBO; 30 sessions) and a 6-week course of antibiotics (clindamycin). Due to the favorable course under this therapeutic regime, major surgical intervention was avoided and the patient experienced a full clinical remission. In the follow-up examination 6 months later the patient was without complaints. Clinical examination revealed no persisting signs of infection. The CT scan performed demonstrated full restitution of bone anatomy in the affected area (Fig. 12.2c).





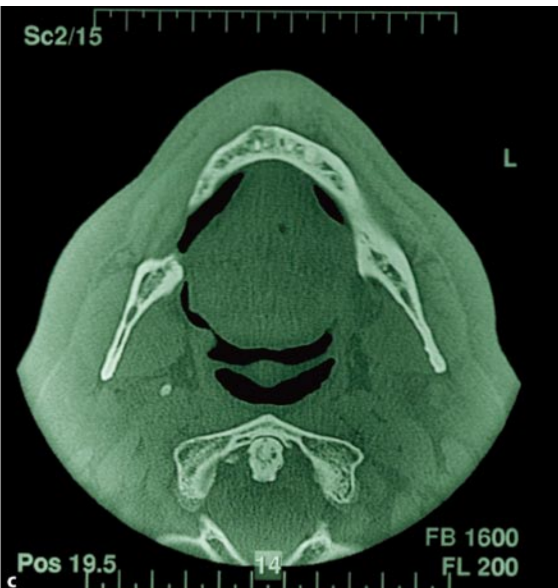


Fig. 12.2a–c Orthopantomography (OPG) 3 weeks after onset of symptoms (**a**). Note the rarefaction of the anterior right corpus. At this point no sequestration is visible. Axial CT scan examination performed 1 day after the OPG shown above (**b**). The rarefaction expands further than suspected on the OPG, up to the middle of the mandibular symphysis. Beginning destruction of the outer cortical bone is notable on the right side. No sequestration is visible at this stage. Axial CT scan taken 6 months after conservative treatment with antibiotics and hyperbaric oxygen therapy (**c**). The rarefaction of bone is beginning to be replaced by normal spongiosa architecture

12.2 Acute Osteomyelitis: Case Reports

12.2.3 Case Report N° 3

Odontogenic Acute Osteomyelitis

Case Report N° 3 – Summary	
Diagnosis	Odontogenic acute osteomyelitis
Affected bone	Left mandibular corpus/angle
Patient	41-year-old woman
General medical history	Uneventful
Dental/maxillofacial-related medical history	Surgical removal of left third molar 1 week prior
Clinical symptoms	Fever Pus discharge from alveolus and beginning submandibular infiltration Strong pain
Treatment	Surgical drainage of submandibular abscess formation Antibiotic therapy Hyperbaric oxygen

A 41-year-old woman was referred by her dentist 1 week after surgical removal of the lower left third molar, after developing a submandibular abscess. Upon presentation she had a submandibular swelling with limited mouth opening and mild fever (38.5°C). The oral exam revealed pus discharge from the alveolus. Initial orthopantomography was adequate without any sign of bone infection (Fig. 12.3a). Surgical drainage of the submandibular abscess from an extraoral approach was performed under general anesthesia. Simultaneous high-dose antibiotics with clindamycin and metronydazol were started. Despite regular salvage of the wound and antibiotic therapy, only an inadequate remission was noted. Upon suspicion of an additional bone infection CT and MRI scans were obtained which confirmed the diagnosis of an acute osteomyelitis of the left mandibular corpus and angle (Fig. 12.3b–d). Additional therapy with HBO (20 sessions) was started immediately and antibiotic drug therapy was continued with clindamycin for a total of 6 weeks. Complete remission was noted with these therapeutic efforts and no further surgical procedure was necessary. A follow-up CT scan after 5 months showed no sign of infection; however, a slight increase of bone sclerosis in the affected region was still noted and interpreted as a bone scar (Fig. 12.3e). The corresponding follow-up MRI showed an almost normal signal intensity of the left mandibular angle compared with the right side (Fig. 12.3f,g).

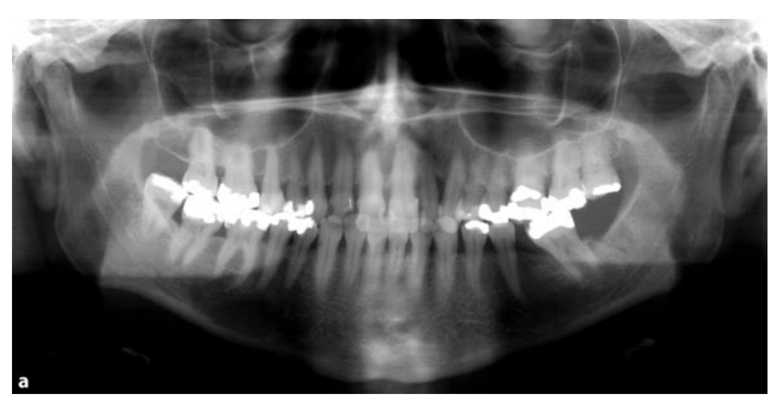






Fig. 12.3a–g Orthopantomography at initial presentation demonstrates normal bone neighboring the extraction site of the lower left molar (**a**). Postoperative CT scan after surgical drainage of the submandibular abscess (**b**). The scan was taken 2.5 weeks after surgical removal of the left third molar. Note the slightly increased sclerosis of the left mandibular angle and the partial osteolysis of the lingual cortical bone corresponding to bone fistula formation (*arrows*). **c,d** Postoperative MRI scans (axial and coronal) after surgical drainage of the submandibular abscess: The scans were taken 2.5 weeks after surgical removal of the left third molar and is the corresponding MRI scan to the CT scan shown in **b**.

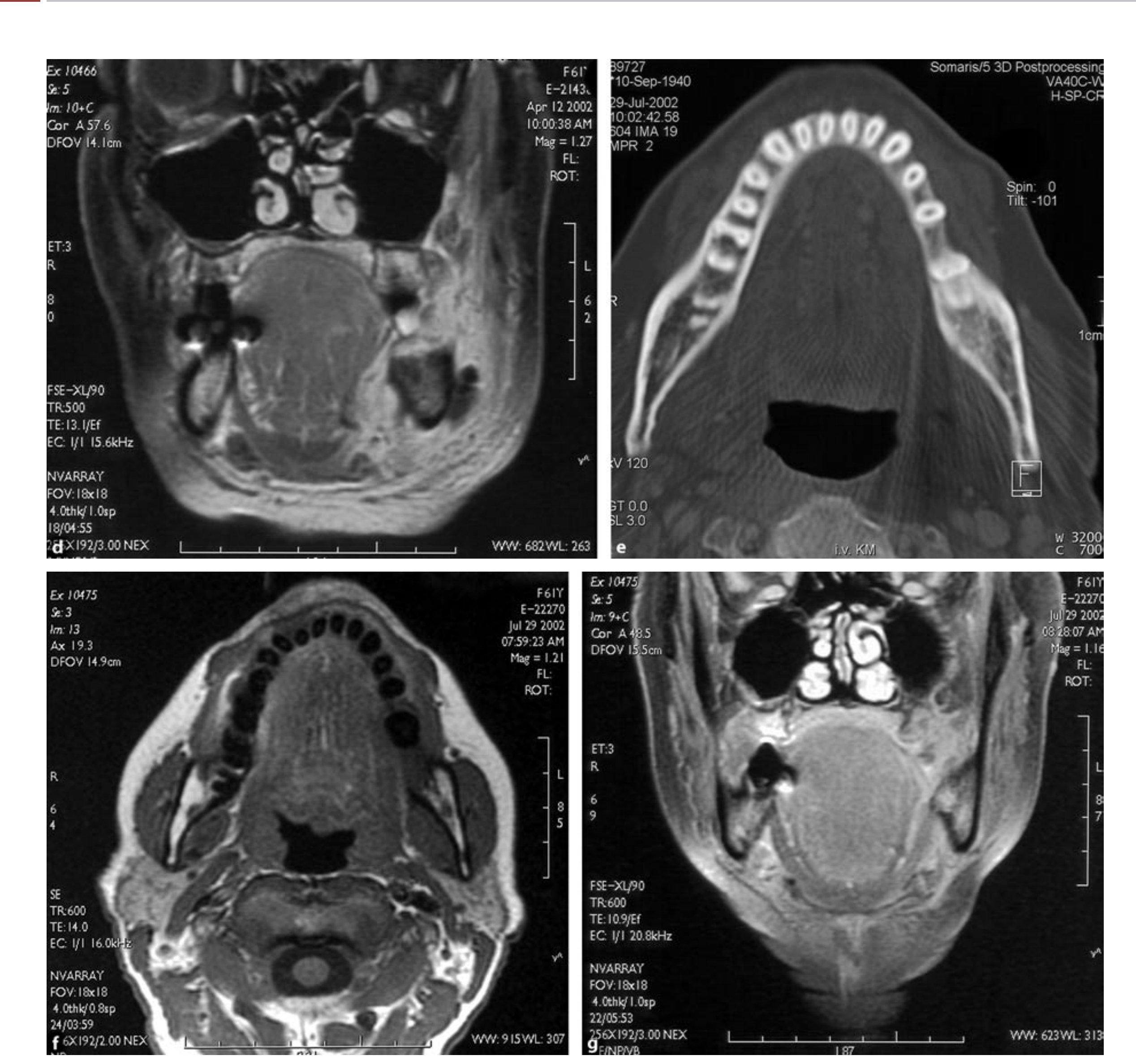


Fig. 12.3a–g (*continued*) **c,d** Postoperative MRI scans (axial and coronal) after surgical drainage of the submandibular abscess: The scans were taken 2.5 weeks after surgical removal of the left third molar and is the corresponding MRI scan to the CT scan shown in **b**. The left mandibular angle demonstrates decreased signal intensity due to decreased local perfusion of the bone. Follow-up CT scan taken 5 months after full clinical remission of the patient (**e**). There is still a slight increased bone sclerosis in the affected region which corresponds to bone scarring, and the lingual cortex in the left angular region still demonstrates some irregularities. Follow-up MRI scans taken 5 months after full clinical remission of the patient (**f,g**). Despite that the signal intensity is still somewhat decreased on the left side compared with the right, the discrepancy is clearly diminished if compared with the acute infectious state (**c,d**)

12.2 Acute Osteomyelitis: Case Reports

12.2.4 Case Report N° 4

Odontogenic Acute Osteomyelitis

Case Report N° 4 – Summary	
Diagnosis	Acute odontogenic osteomyelitis (advanced stage)
Affected bone	Right mandible
Patient	47-year-old woman
General medical history	Light asthma
Dental/maxillofacial-related medical history	Extraction of infected right-sided lower second molar 2 weeks prior to referral Clinical and radiological signs of regional periodontal disease
Clinical symptoms	Dull pain right mandible Strongly reduced sensitivity of the right lower alveolar nerve (Vincent's symptom)
Treatment	Surgical decortication Antibiotic therapy

A 47-year-old woman was referred from her family dentist with a slowly healing extracting wound after having her infected lower right second molar extracted with a forceps as an emergency procedure elsewhere 3 weeks prior. Besides a dull pain in her right lower jaw, the patient's chief complaint was an increasing numbness of her lower right lip, which had begun within days after the extraction procedure. Clinical examination revealed an extraction socket of her lower right second molar in an advanced healing stage. No abscess or fistula formation was present. No notable swelling of the mandible was noted; however, the right mandible was somewhat tender on palpation. An approximately 2×4 cm large area of her lower right lip and chin area (Fig. 12.4a) demonstrated severe hypoesthesia, as did the vestibular gingiva of the lower right jaw. Furthermore, molar and premolar teeth of the lower right jaw were negative on vitality probing. Initial orthopantomography showed an extraction socket of the lower right second molar with normal architecture of the surrounding bone (Fig. 12.4b). Further diagnostic work-up included MRI and CT imaging studies: MRI revealed somewhat decreased signal intensity on the T1-wighted images with buccal cortical irregularities in the region of the lower right second molar (Fig. 12.4c,d). After administration of contrast medium, an increased signal intensity was noted in the right lower jaw from the second molar up to the right canine region. Marked increase of contrast medium was especially noted along the neurovascular bundle (Fig. 12.4e,f). Corresponding CT scans demonstrated a sequester formation next to the mandibular canal apical to the alveolus of the second lower right molar with some local osteolysis (Fig. 12.4g,h).

After establishing the diagnosis of advanced-stage acute osteomyelitis, therapy was initiated consisting of surgical decortication (Fig. 12.4i,j) and antibiotics (clindamycin) for a 6-week period. In the follow-up the patient experienced a full remission with completely restored sensory function of the inferior alveolar nerve after a 4-month period (Fig. 12.4k). A follow-up CT scan showed a right mandible after decortication with no residual signs of infection and normal architecture of the remaining cortical and spongious bone of the mandible (Fig. 12.4l,m).



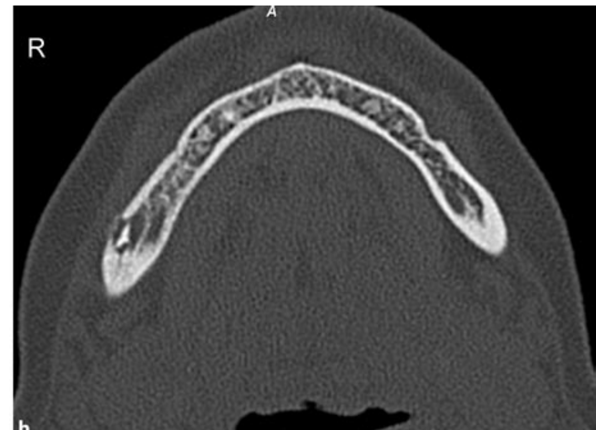


Fig. 12.4a–m Patient at initial presentation demonstrates a 2 × 4-cm-large area of strong hypoesthesia of the lower right lip (**a**). Orthopantomography at initial presentation of the patient shows the extraction alveolus of the lower second molar with normal surrounding bone architecture (**b**). **c–m** *see next page*



Fig. 12.4a–m (*continued*) The MRI scans (T1-weighted native scans) at initial presentation (**c,d**). There is somewhat decreased signal intensity in the T1-wighted images with buccal cortical irregularities in the region of the lower right second molar. The MRI scans (T2-weighted scans with contrast) at initial presentation) (**e,f**). An increased signal intensity is noted in the right lower jaw from the second molar up to the right canine region. Marked increase of contrast medium is especially noted along the neurovascular bundle. **g–m** *see next page*





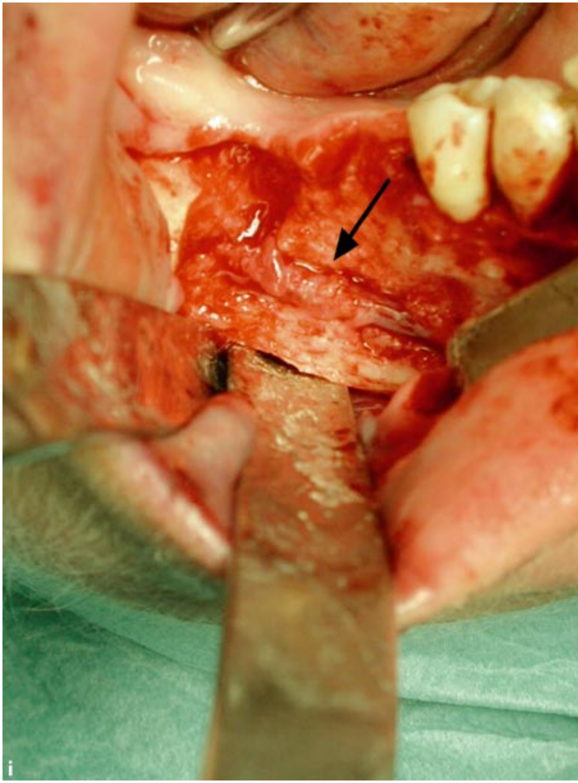


Fig. 12.4a–m (*continued*) **g,h** The CT scans corresponding to the MRI scans demonstrated in **c–f**: Advanced-stage acute osteomyelitis of the molar region of the right mandible. A single sequester and osteolysis can be seen vestibular to the mandibular canal apical to the extraction socket of the second molar. The buccal cortex is disrupted in the region of the sequester. Intraoperative view after surgical decortication and removal of the lower first molar (**i**). Note the granule tissue around the neurovascular bundle which shows a marked degree of edema (*arrow*). **j–m** *see next page*





Fig. 12.4a–m (*continued*) Postoperative orthopantomography after surgical decortication of the lower right mandible and removal of the first lower right molar (**j**). Patient 3 weeks after surgical decortication (**k**). Marked remission of sensory function is already noted. **l–m** *see next page*

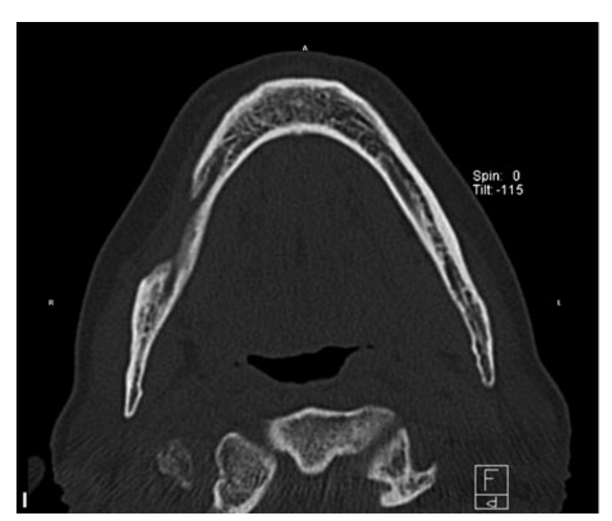




Fig. 12.4a–m (*continued*) Follow-up CT scans 4 months after surgical decortication of the right mandible. The remaining cortical bone and spongiosa demonstrate a normal architecture with no remaining signs of active infection. Axial (**l**) and corresponding coronal scan (**m**). Intraoperative view after surgical decortication and removal of the lower first molar (**i**). Note the granule tissue around the neurovascular bundle which shows a marked degree of edema. Postoperative orthopantomography after surgical decortication of the lower right mandible and removal of the first lower right molar (**j**). Patient 3 weeks after surgical decortication (**k**). Marked remission of sensory function is already noted. Follow-up CT scans 4 months after surgical decortication of the right mandible. The remaining cortical bone and spongiosa demonstrate a normal architecture with no remaining signs of active infection. Axial (**l**) and corresponding coronal scan (**m**)

12.3 Secondary Chronic Osteomyelitis: Case Reports

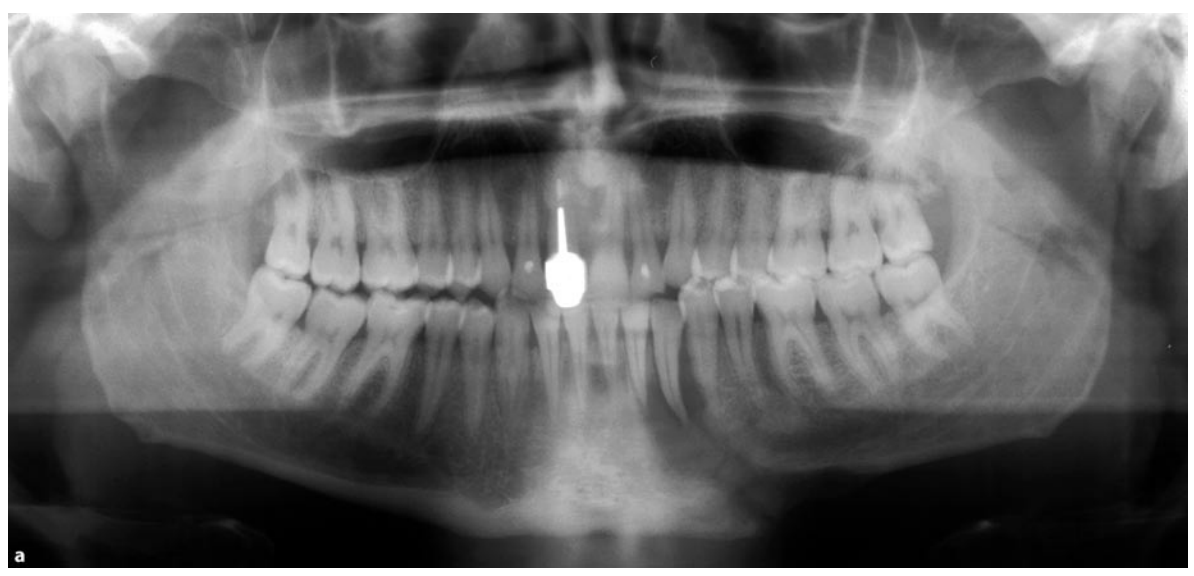
12.3.1 Case Report N° 5

Trauma/Fracture-related Secondary Chronic Osteomyelitis

Case Report N° 5 – Summary	
Diagnosis	Trauma/fracture-related secondary chronic osteomyelitis Infected nonconsolidated fracture of the left mandibular body Consolidated, non infected fracture of the left ascending ramus
Affected bone	Left mandibular corpus
Patient	29-year-old man
General medical history	IV drug abuse
Dental/maxillofacial-related medical history	Blow toward the left side of the mandible 2.5 months prior to first presentation to a health care professional
Clinical symptoms	Increasing pain Oral fistula formation with pus discharge Instable mandible with malocclusion
Treatment	Surgical debridement including extraction of the canine, local decortication and osteosynthesis with reconstruction plate Reconstruction of the bony defect with an autologous bone graft from the iliac crest Antibiotic therapy

A 29-year-old man with a history of drug abuse experienced a blow to his lower left jaw 2.5 months prior. The patient did not seek medical treatment initially. For 2 weeks he complained of increasing pain with discharge of pus into the oral cavity from the fracture site. At his first clinical presentation an instable fracture of the left paramedian region of the mandible was diagnosed, which was confirmed on conventional radiographs (Fig. 12.5a,b). Oral fistula formation and suppuration was noted at the fracture site in the region of the lower left canine. An additional noninfected and mostly consolidated fracture of the right ascending ramus was noted. Further radiological work-up with CT and MRI scans confirmed the suspected diagnosis secondary chronic osteomyelitis (Fig. 12.5c–e).

Surgical therapy consisted of extensive local debridement, including extraction of the canine, local decortication, and stabilization of the fracture by osteosynthesis with a 2.4-mm reconstruction plate (Fig. 12.5f). The fracture of the ascending ramus already showed sufficient consolidation; hence, no additional therapy was necessary. Postoperative short-term antibiotics for 3 weeks were administered with amoxicillin/clavulanic acid. After complete remission, the remaining bone defect was reconstructed 6 months later with an autologous bone graft from the iliac crest, which showed an uneventful healing. The reconstruction plate was left in place to guarantee a stable healing environment for the bone graft (Fig. 12.5g).





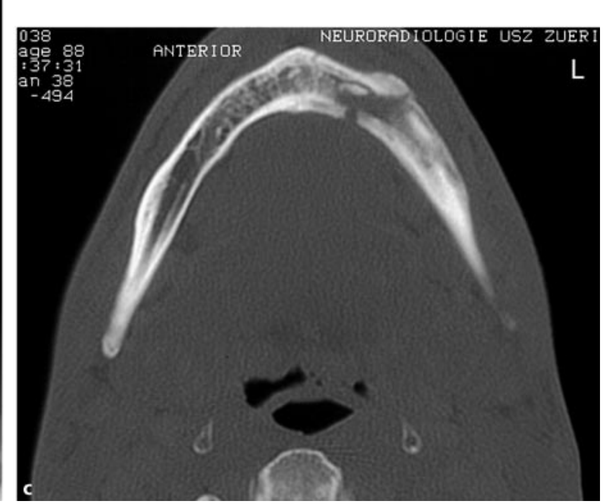
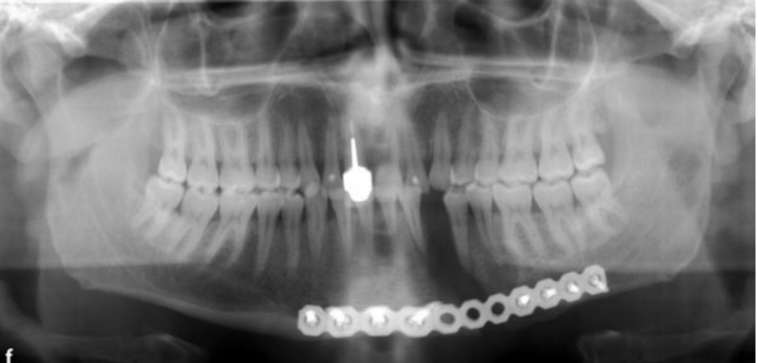


Fig. 12.5a–g Orthopantomraphy shows a dislocated fracture of the left-sided canine region of the lower jaw with adjunctive osteolysis (**a**). The left canine lies within the fracture gap. An additional mostly consolidated fracture is noted in the right ascending ramus. Clementschich image shows the dislocated fracture in an anteroposterior view (**b**). Axial CT scans demonstrate a nonunified mandibular fracture (**c,d**). **d–g** *see next page*





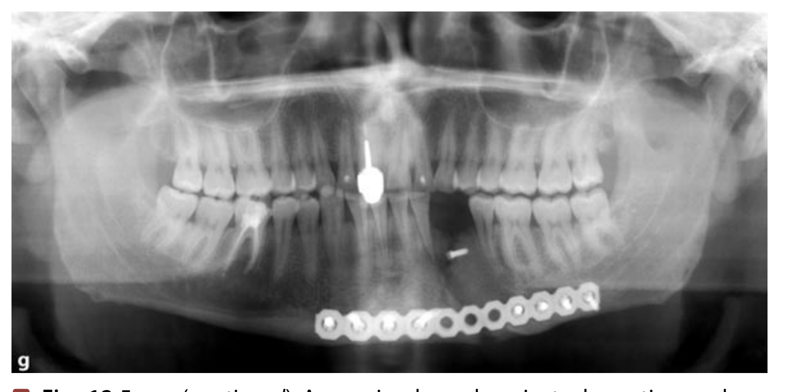


Fig. 12.5a–g (*continued*) A massive buccal periosteal reaction and osteolysis with sequester formation are indicative for chronic osteomyelitis. **e** Axial MRI of the mandible corresponding to the CT scans in **c** and **d**. Note the decreased signal intensity in the anterior mandible, indicating the reduced local perfusion of the infected bone. Orthopantomraphy of the same patient after surgery (**f**). The infected bone was removed and the left lower canine extracted. The resulting gap is bridged with a 2.4-mm reconstruction plate. Postoperative orthopantomography after local reconstruction with an autologous bone graft taken from the iliac crest (**g**). The bone graft was fixed locally with a 12-mm 2.0-mm mini-screw. The reconstruction plate was left in position to ensure a stable healing environment for the bone graft

12.3 Secondary Chronic Osteomyelitis: Case Reports

12.3.2 Case Report N° 6

Odontogenic Secondary Chronic Osteomyelitis

Case Report N° 6 – Summary	
Diagnosis	Odontogenic secondary chronic osteomyelitis
Affected bone	Left mandible
Patient	43-year-old man
General medical history	Unspecific
Dental/maxillofacial-related medical history	Prior endodontic treatment of the first lower left molar 8 weeks prior to initial presentation
Clinical symptoms	Hard swelling and mild pain of the left mandible Hypoesthesia of the left mental nerve second premolar demonstrating negative vitality testing First and second left molar demonstrating increased mobility (grades II–III) with local fistula formation Limited jaw opening
Treatment	Surgical decortication and removal of affected teeth Intermaxillary fixation Hyperbaric oxygen Antibiotic therapy

A 43-year-old man was referred from his dentist with a hard swelling a mild pain of his left lower jaw. His dental history revealed an uncompleted endodontic treatment of the first lower left molar approximately 8 weeks prior. The general medical history was uneventful.

Initial presentation showed a hard, somewhat painful swelling of the left mandible. Neurosensory function of the left inferior alveolar was decreased (Vincent's symptom). Oral examination demonstrated an increased mobility of the first lower left molar with local fistula formation (Fig. 12.6b). The second left lower premolar was negative on vitality testing. Initial orthopantomography revealed massive osteolysis with intermittent sclerosis in the region of the left lower mandible (Fig. 12.6a). Corresponding CT scans then demonstrated the full extension of the lesion with all classical radiological signs of extensive secondary chronic osteomyelitis of the left mandibular body (Fig. 12.6c–h). Bone scans showed a strong increase in activity in the entire left mandible (Fig. 12.6i).

Surgical therapy consisted of decortication with removal of all infected bone and granulation tissue with subsequent neurolysis of the inferior alveolar nerve. The impacted third left lower molar was not affected by the infection and left in place to avoid further weakening of the mandible, whereas the second premolar and the first and second left lower molars needed to be removed (Fig. 12.6j). To stabilize the mandible osteosynthesis was performed with two miniplates and the mandible immobilized with additional maxillomandibular (intermaxillar) fixation (MMF/IMF; Fig. 12.6k) for 6 weeks. Postoperative HBO with a total of 30 sessions in the HBO chamber and a prolonged antibiotic therapy with clindamycin (3×300 mg/day) for 12 weeks were additionally included in the therapeutic regimen for this patient. Follow-up CT scans after 6 months demonstrated significant bone remodeling with absence of signs of infection.







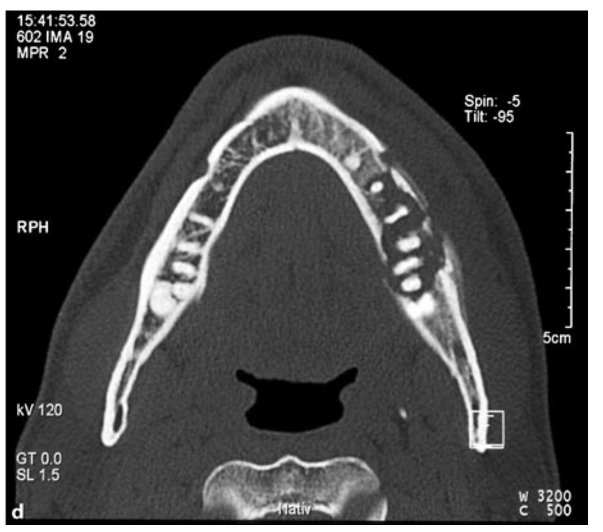


Fig. 12.6a–m Orthopantomogram of the patient on a first presentation (**a**). Note the massive osteolysis with intermittent sclerosis in the region of the left lower mandible. Oral examination at first presentation (**b**). There is a fistula formation and swelling in the vestibule of the lower left first molar, where root canal therapy was started. Computed tomography scans (axial view) at first presentation demonstrate massive destruction of the left mandible with significant osteolysis and sequester formation (**c**,**d**). The molar teeth are fully embedded in the granulation and infected tissue. A strong periosteal reaction on the buccal aspect of the mandible is evident with formation of a neocortex. **e**–**m** *see next page*

■ **Fig. 12.6a–m** (*continued*) **e,f** Corresponding coronal views to **c** and **d**. **g,h** Corresponding sagittal views to **c** and **d**: The osteolysis alongside the mandibular canal is impressive in **g,h** demonstrating a primary pathway for the spreading of the bone infection. Bone scan at first presentation shows a strong increase in activity in the entire left mandible (**i**).Surgically removed first lower left molar (**j**). **k–m** *see next page*



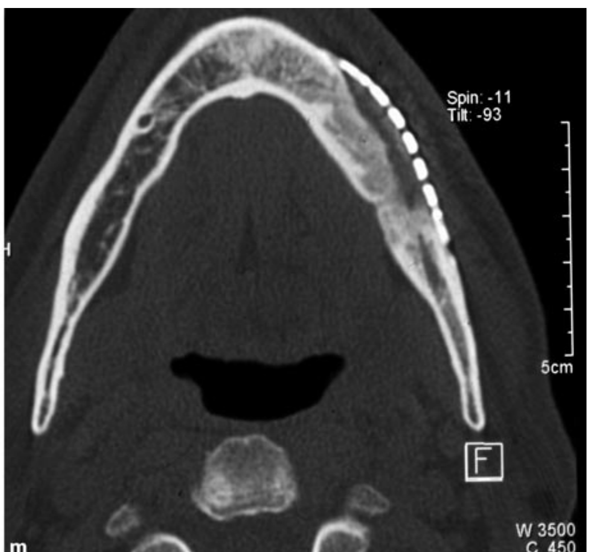


Fig. 12.6a–m (*continued*) The tooth and the remaining attached bone formed a sequester surrounded by granulation tissue, with no remaining contact to the mandibular bone. Postoperative orthopantomography after surgical debridement and decortication in the left mandible with removal of the second premolar as well as the first and second molar teeth (**k**). The left third molar was not involved in the infected area and hence was left remaining for stability reasons. The left mandible is stabilized by intact remaining lingual cortical bone, two 2.0-mm miniplates, and an intermaxillary fixation (see text). **l** Postoperative CT scan corresponding to **k** demonstrates the extent of the surgical debridement in the axial plane. Follow-up CT scans 6 months after surgery and completion of hyperbaric and antibiotic therapy. Note the significant bone remodeling which has taken place (**m**)

12.3.3 CASE REPORT N° 7

Odontogenic Secondary Chronic Osteomyelitis

Case Report N° 7 – Summary	
Diagnosis	Odontogenic secondary chronic osteomyelitis
Affected bone	Right mandible
Patient	65-year-old man
General medical history	Regular cigar smoking Moderate alcohol consumption
Dental/maxillofacial-related medical history	Severe generalized periodontal disease Extraction of multiple periodontal strongly affected teeth 5 weeks prior to admission
Clinical symptoms	Hard swelling and pain of the right mandible Hypoesthesia of the right mental nerve (Vincent's symptom) Oral fistula formation in the right mandible Poor/nonhealing extraction sockets in the right mandible
Treatment	Extraoral abscess incision ad drainage Antibiotic therapy Decortication and neurolysis of the inferior alveolar nerve, osteosynthesis of the mandible Antibiotic therapy and hyperbaric oxygen Partial resection of the left mandible and simultaneous reconstruction with a free osseomyocutaneous fibula flap Antibiotic therapy

A 65-year-old man was admitted to the hospital by his family dentist with a strong and painful selling of the right mandible/submandibular region. His medical history revealed that 5 weeks prior, several periodontal strongly affected teeth in the anterior and left mandible were extracted. Despite a more than 4-week course of antibiotics (amoxicillin), the swelling and pain had continuously increased. The patient regularly smoked cigars and moderately consumed alcohol.

At first presentation the patient was moderately compromised with fever (38.5°C). A painful perimandibular swelling with strong inflammation was noted indication a peri-/submandibular abscess formation. A slight hypoesthesia of the right alveolar nerve was further noted (Vincent's symptom). Intraoral examination was difficult due to limited mouth opening and revealed multiple extraction sockets with poor healing and local fistula/pus formation.

Initial orthopantomography already demonstrated osteolysis in the anterior part of the mandible, highly suspicious for additional osteomyelitis aside from the abscess formation (Fig. 12.7a). Due to the extension of the abscess formation, surgical incision and drainage by extraoral approach was conducted without further delay and postoperative antibiotic therapy started with clindamycin. The drained abscess was regularly irrigated with neomycin solution.

In the follow-up CT scans were obtained that revealed sequester formation and periosteal reaction confirming the suspected diagnosis secondary chronic osteomyelitis (Fig. 12.7b–d). After remission of the acute infection, surgical debridement of the infected bone was performed by decortication, sequestrectomy removal of periosteal bone formation. During this procedure the inferior alveolar nerve which was running through the infected bone was freed in a lateral neurolysis procedure. To stabilize the weakened mandible a thick plate was administered to the remaining right mandible (Fig. 12.7e–j).

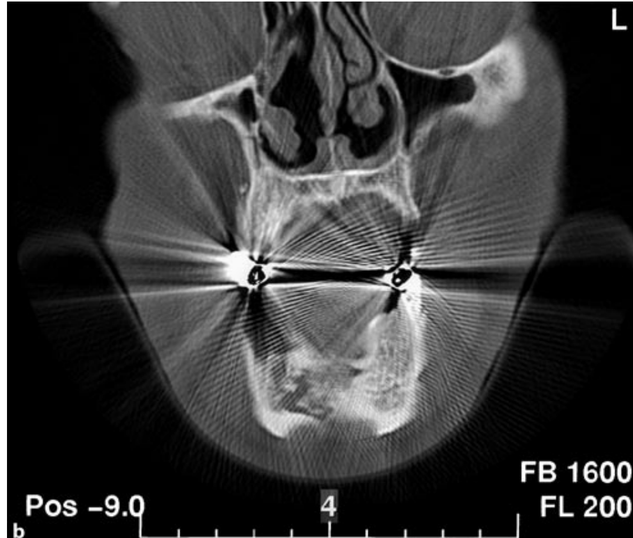
Postoperative treatment consisted of continua-

tion of the antibiotic therapy (clindamycin) and a total of 30 sessions in the HBO chamber. Despite these adjuvant measures, pain and swelling did not subside adequately after a period of 5 weeks; hence, follow-up CT scans were obtained showing rapid further progression of the infection to the base of the right mandible (Fig. 12.7k,l).

In conclusion, of the course and extent of the osteomyelitis resection of the entire infected right and anterior part of the mandible was necessary (Fig. 12.7m). The remaining mandible was stabilized with a reconstruction plate and the bone and soft tissue defect simultaneously were reconstructed with a free osteomyocutaneous fibula flap (Fig. 12.7n–r). Short-term postoperative antibiotics (clindamycin) for 3 weeks were administered. The further postoperative course was uneventful.

The 2-month follow-up showed a very well-perfused microvascular flap and no remaining clinical sign of infection (Fig. 12.7s,t,u), allowing further prosthodontic rehabilitation.





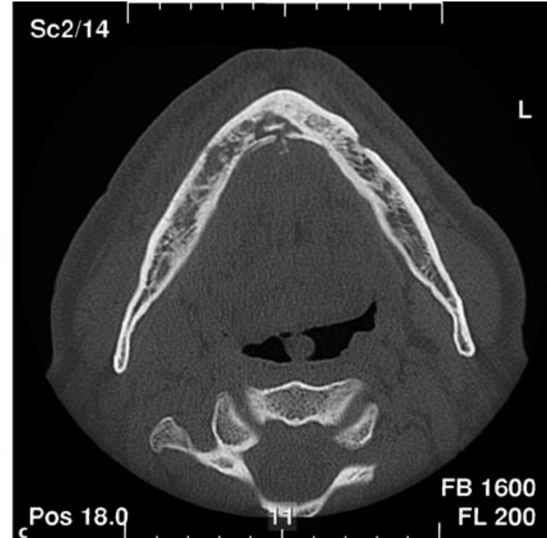


Fig. 12.7a–u Orthopantomogram at first presentation 5 weeks after the patient's dentist removed several teeth with severe periodontal disease (**a**). Beginning osteolysis of the structure can already be noted in the anterior part of the right mandible. A CT scan (coronal view) at first presentation (**b**). A CT scan (axial view) at first presentation (**c**,**d**). **d–u** *see next page*

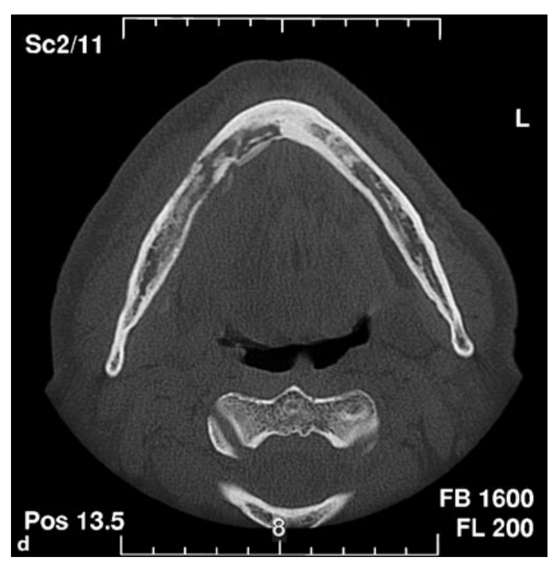
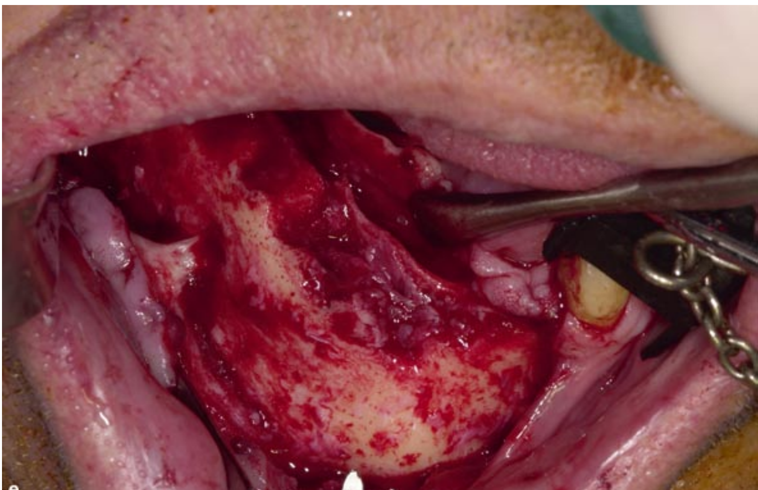
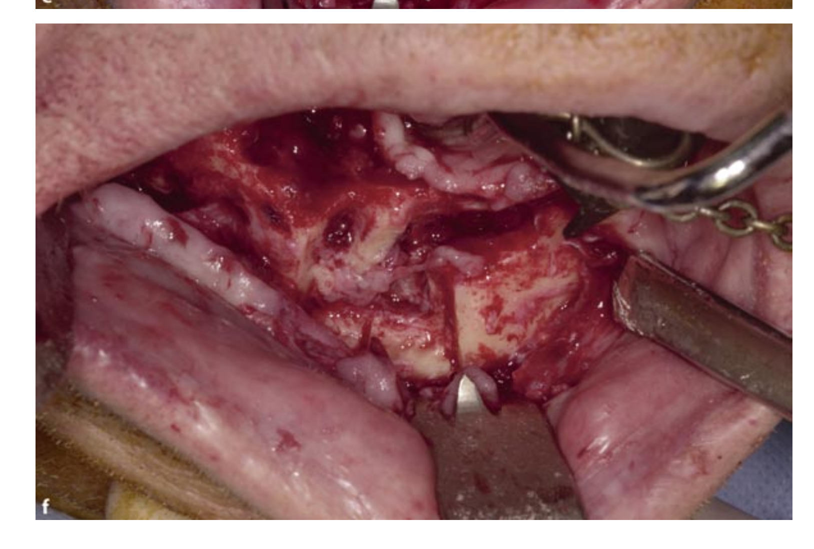
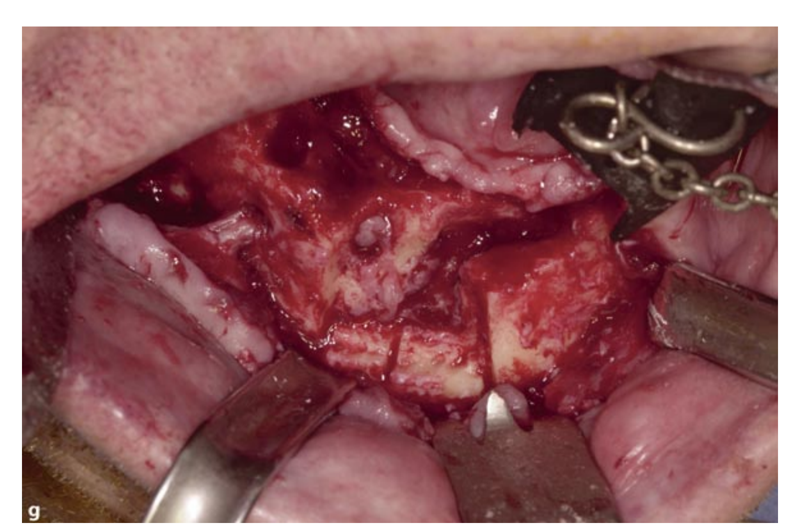
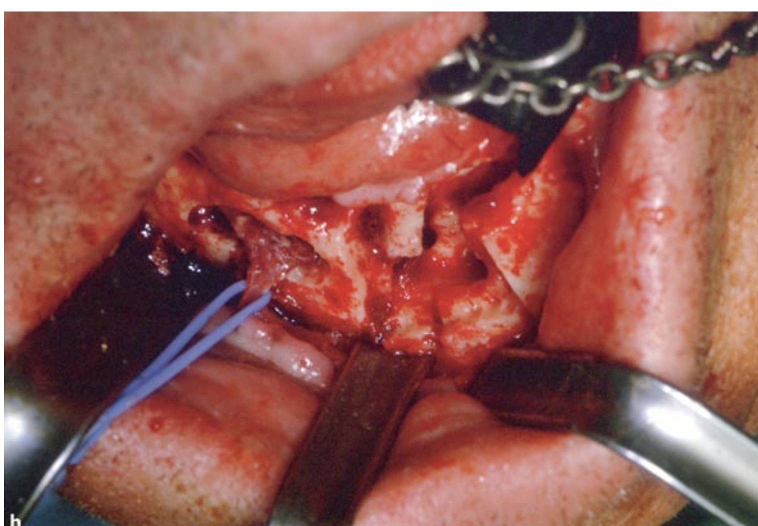


Fig. 12.7a–u (*continued*) A CT scan (axial view) at first presentation (**c,d**). Strong osteolysis and sequester formation is noted in the anterior right mandible. The periosteal reaction is confined mainly to the lingual cortex. **e–h** Intraoperative views of the first debridement procedure: operative view after removal of the mucoperiosteal flap (**e**). The mental nerve is dissected to the left. Note the large amount of granulation tissue within the alveoli. Begin with buccal decortication in the anterior part of the mandible which reveals the extent of the infected tissue (**f**). **g–u** *see next page*









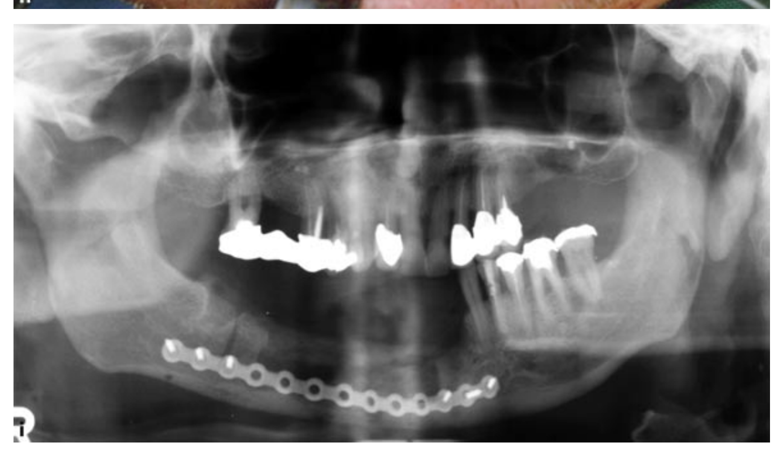
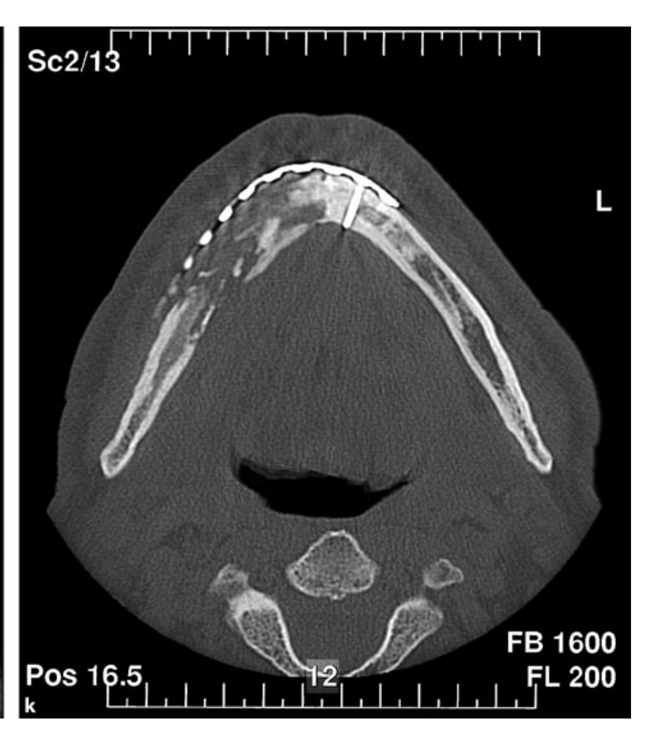


Fig. 12.7a–u (*continued*) The granulation tissue has been partially removed **e–h** Intraoperative views of the first debridement procedure: The granulation tissue has been partially removed (**g**). Surgical site after completed debridement and partial neurolyses of the mental nerve which is partially retracted by a vessel loop (**h**). Postoperative orthopantomography and Clementschich view (**i,j**). **j–u** *see next page*





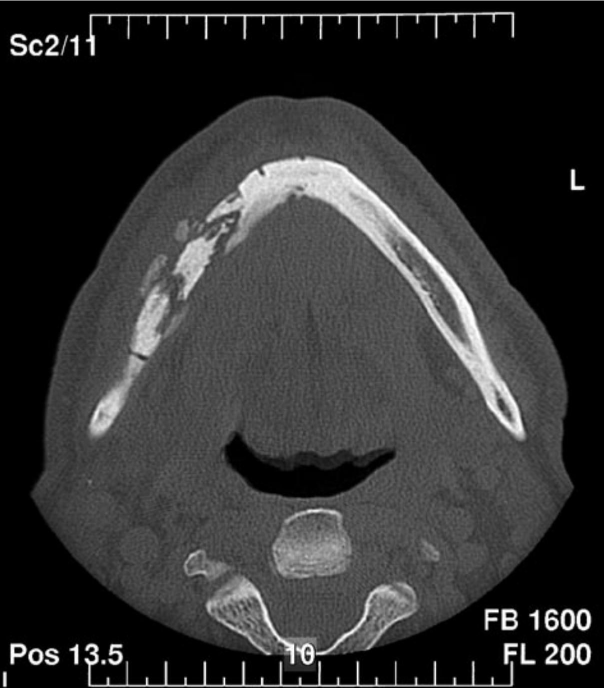


Fig. 12.7a–u (*continued*) The mandible is stabilized with a reconstruction plate. The CT scans (axial view) after 1-month follow-up (**k,l**). There is clear progress of the bone infection noted on the lingual cortex and at the base of the mandible with formation of a large sequester. **m–u** *see next page*







Fig. 12.7a–u (*continued*) Surgical specimen of the resected mandible with adjacent granulation tissue (**m**). Intraoperative view after resection of the infected mandible and stabilization of the remaining mandibular parts with a reconstruction plate (**n**). Harvested fibula composite graft with microvascular attached adjacent skin (**o**). **p–u** *see next page*

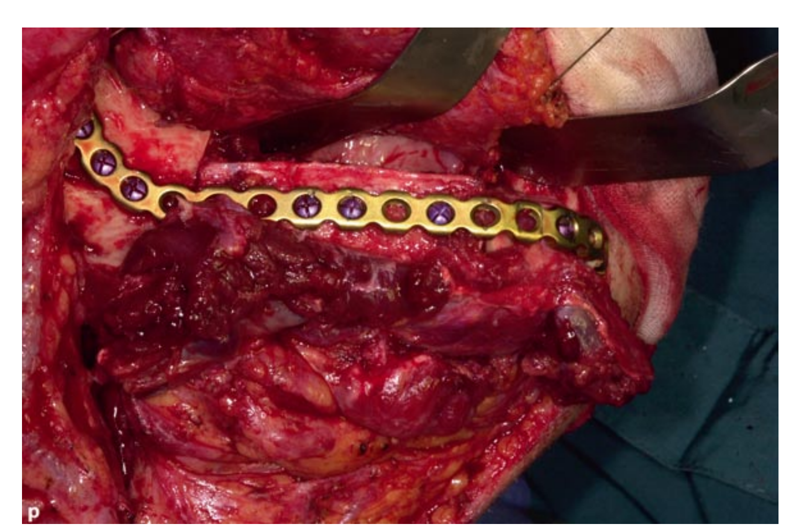






Fig. 12.7a–u (*continued*) Intraoperative view after positioning and stabilization of the fibula composite graft (**p**). Postoperative orthopantomography and Clementschich view (**q**,**r**). **s**-**u** *see next page*

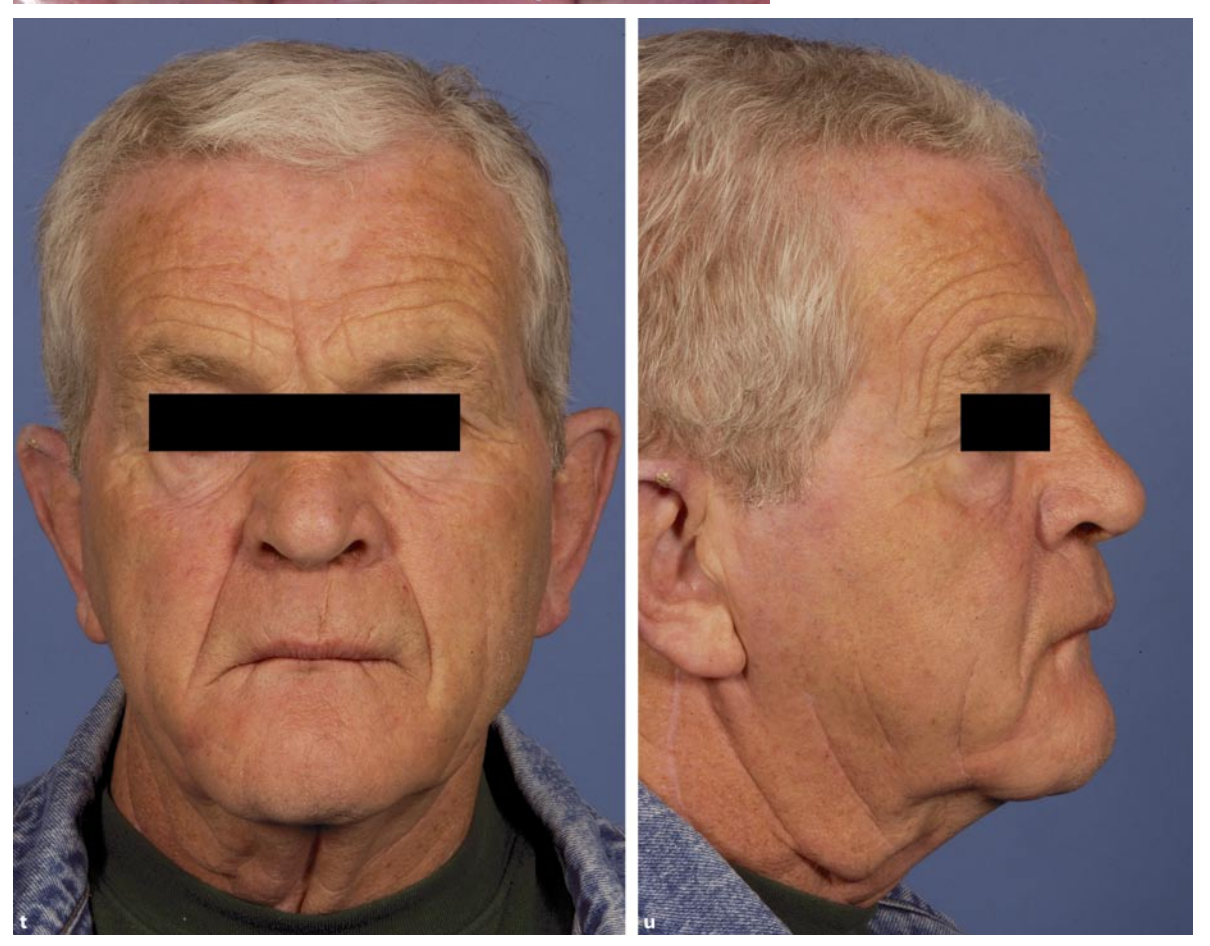


Fig. 12.7a–u (*continued*) Intraoral view 2 months postoperative with a healed, well-perfused microvascular skin flap and no remaining clinical sign of infection (**s**). Patient 2 months postoperative (**t,u**; anteroposterior and lateral view)

12.3.4 Case Report N° 8

Odontogenic Secondary Chronic Osteomyelitis with Involvement of the Condyle

Case Report N° 8 – Summary	
Diagnosis	Odontogenic secondary chronic osteomyelitis with involvement of the condyle
Affected bone	Right condyle
Patient	25-years-old man
General medical history	Uneventful
Dental/maxillofacial-related medical history	Diagnosed and treated (decortication) secondary chronic osteomyelitis following extraction of the right lower third molar
Clinical symptoms	Diffuse swelling of the right perimandibular and preauricular region Paraesthesia of the right interior alveolar nerve (Vincent's symptom) Limited mouth opening (29-mm intercanthal space)
Treatment	Temporary MMF Antibiotic therapy and hyperbaric oxygen Partial resection of the right mandible including the right condyle and simultaneous reconstruction with free vascular fibula graft Intensive postoperative physiotherapy Antibiotic therapy

A 25-year-old man was admitted to the hospital with a painful swelling in the right temporomandibular joint (TMJ) region. Clinical examination revealed a well-conditioned patient with a diffuse swelling of the right perimandibular and preauricular region. A reduced mouth opening of 29-mm intercanthal space and a slight paraesthesia of the right inferior alveolar nerve (Vincent's symptom) were further noted (Fig. 12.8a,b). Neither abscess- or fistula formation were evident. Six weeks prior to admission, the patient had already undergone a decortication procedure of the right mandibular angle in his home country, due to secondary chronic osteomyelitis of the right mandible following extraction of the lower right third molar.

The CT scans demonstrated irregular radiolucencies in the right mandibular angel, the ascending ramus, and the mandibular condyle. Additionally, two fracture zones in the ascending ramus and the condyle were noticed (Fig. 12.8c).

In order to splint the fractures, initially maxillomandibular wire fixation (MMF) was performed (Fig. 12.8d,e). During the same procedure bone biopsies were performed which confirmed the diagnosis of a chronic suppurative bone infection corresponding secondary chronic osteomyelitis. After the biopsy, the patient was immediately started on high-dose intravenously administered antibiotics with amoxicillin/clavulanic acid and metronidazole, and HBO therapy (20 sessions) were initiated. During this time the patient remained in MMF. After preconditioning the tissue with HBO, partial surgical resection of the right hemimandible and simultaneous reconstruction with a microvascular free fibular graft was performed. Postoperative short-term antibiotics were continued for 2 weeks until wound healing was assured. Physiotherapy was applied to support the patient in achieving normal masticatory function. Six months after surgery, the patient was free of pain and able to eat solid food. Mouth opening returned to almost normal function with a measured intercanthal space of now 45 mm (Fig. 12.8f). The follow-up images demonstrated osseous union between the graft and the mandible (Fig. 12.8g,h).

A summary of case report 8 is given in Table 12.8.

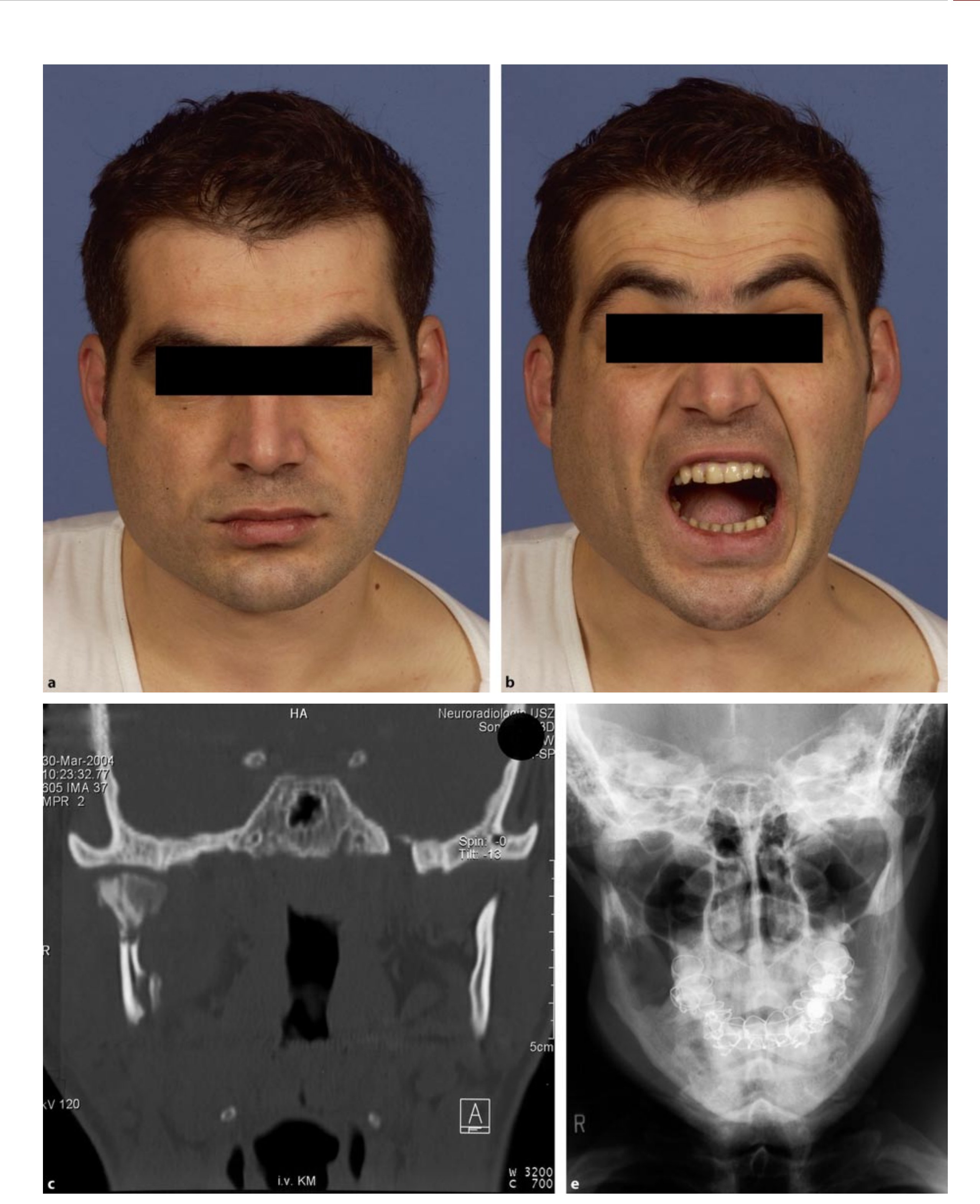
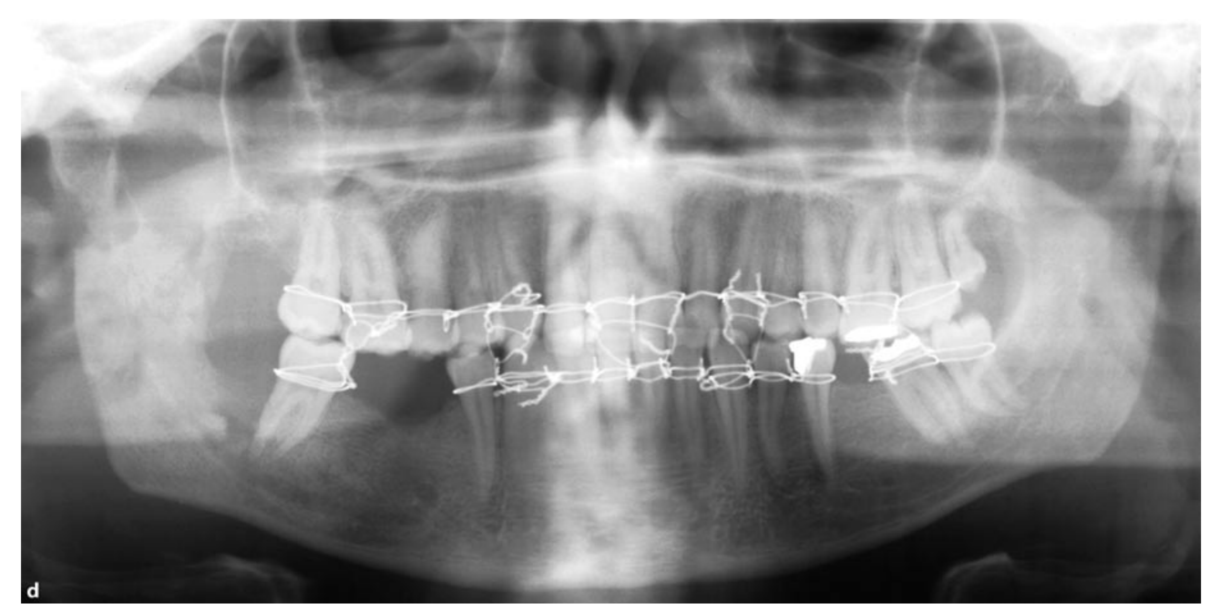


Fig. 12.8a–h Patient at initial presentation with painful swelling of the right mandible up to the preauricular region and trismus with limited mouth opening of approximately 25-mm intercanthal distance (**a**,**b**). A CT scan (coronal view) of the patient at initial presentation (**c**). The right condyle demonstrates two fracture zones and a periosteal reaction on the lateral aspect. Orthopantomography and anteroposterior view after temporary maxillomandibular fixation using Obwegeser ligatures and biopsy procedure (**d**,**e**). **e–h** *see next page*



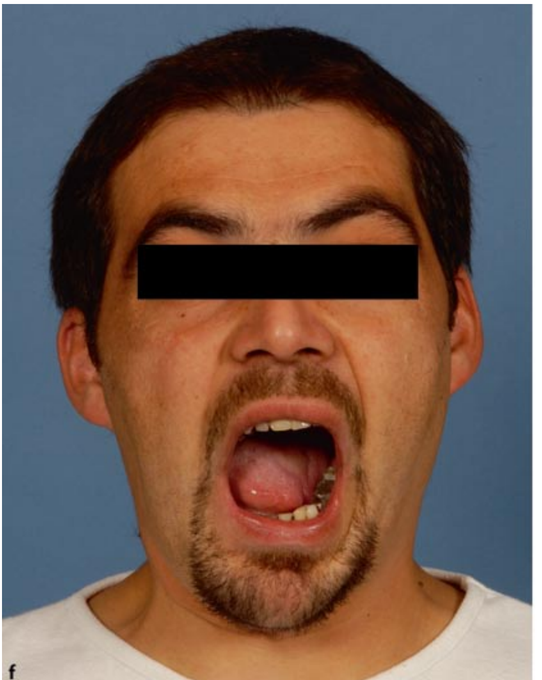




Fig. 12.8a–h (*continued*) Note the severe radiolucencies in the right ascending ramus and condyle. Patient 6 months after surgery with an almost normal mouth opening with an intercanthal space of 45 mm (**f**). Orthopantomography and anteroposterior view 6 months after partial resection of the right mandible/condyle and simultaneous reconstruction with a vascularized fibular graft (**g,h**). The distal end of the fibular graft was used to form a new condyle. **g** *see next page.*

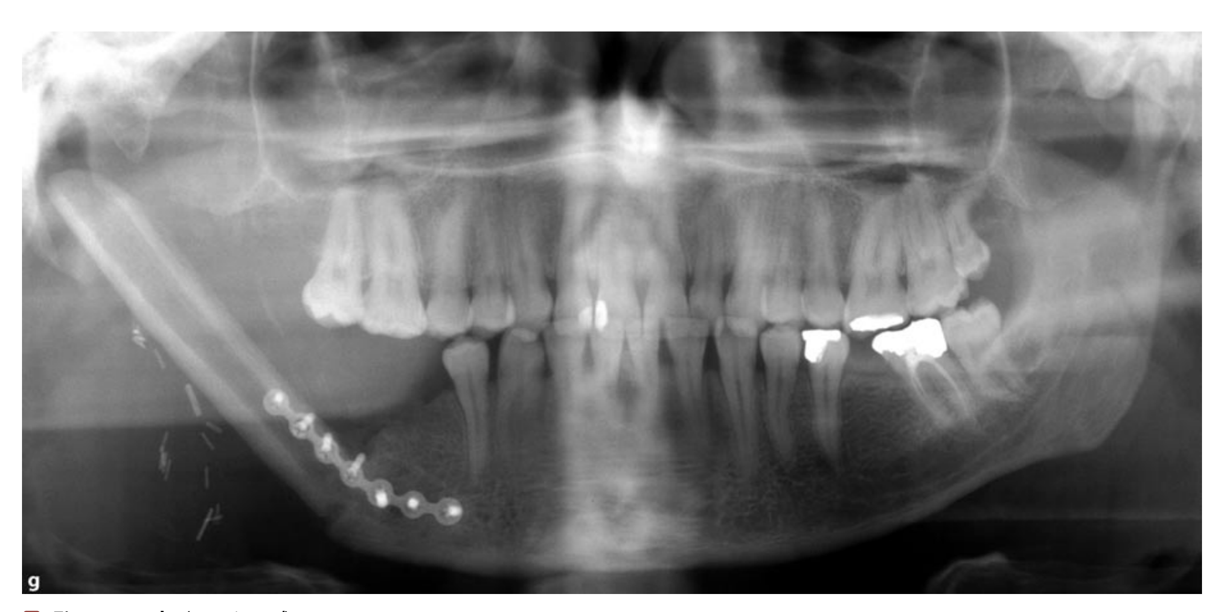


Fig. 12.8a–h (*continued*)

12.3 Secondary Chronic Osteomyelitis: Case Reports

12.3.5 Case Report N° 9

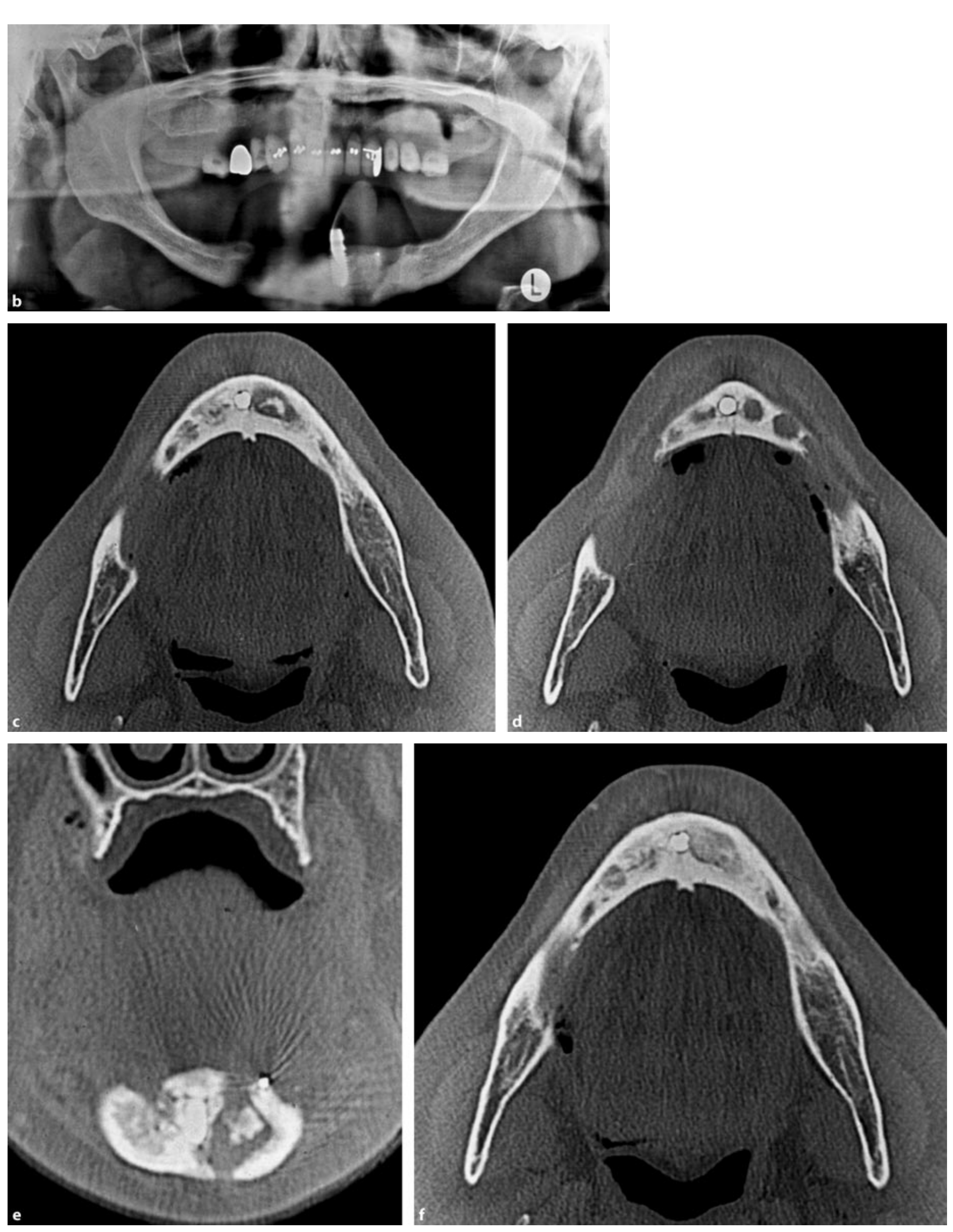
Foreign Body, Transplant/Implant-induced Secondary Chronic Osteomyelitis

Case Report N° 9 – Summary	
Diagnosis	Implant-induced secondary chronic osteomyelitis
Affected bone	Anterior mandible
Patient	75-year-old woman
General medical history	Uneventful
Dental/maxillofacial-related medical history	Implant placement in the anterior mandible several years prior
Clinical symptoms	Pain, swelling, and local abscess formation submental
Treatment	Abscess incision and drainage, removal of infected dental implants, minor surgical debridement (first surgery) Antibiotic therapy Major debridement, sequestrectomy and local decortication, placement of lyophilized cartilage (second surgery) Antibiotic therapy and hyperbaric oxygen

A 75-year-old woman presented with chronic periimplantitis in the lower canine region (Fig. 12.9a). For 4 days she had noted an increasing pain and submental swelling. A submental abscess was diagnosed and treated surgically. The infected implant was removed simultaneously, and antibiotics were administered for 3 weeks. During her follow-up two further implants with critical prognosis were removed by her dentist (Fig. 12.9b). After a period of remission, the patient was referred again 10 months later with another abscess in the same region. A CT examination revealed a chronic osteomyelitis with sequester formation (Fig. 12.9c–e). Removal of granulation tissue and sequester and decortication were performed. To stabilize the brittle bone, defects were filled up with lyophilized cartilage. Supplemental therapy consisted of a 6-week course of antibiotics (clindamycin) and treatment in the HBO chamber (20 sessions). A significant clinical improvement was noted in the follow-up with no signs of relapse. The most recent CT, taken 7 months after the second surgical intervention, showed no signs of infection and an advanced sclerosis of the cartilage implants (Fig. 12.9f).



Fig. 12.9a–f Orthopantomography demonstrates a prominent osteolysis around the distal left-sided implant which was considered the primary source of infection (**a**). Note that also the other implants show moderate to severe osteolysis consistent with periimplantitis. **b–f** *see next page*



◘ **Fig. 12.9a–f** (*continued*) Orthopantomography 6 months after initial surgical therapy (**b**). The infected implants were removed. Computed tomography scans of the patient 10 months after initial surgery (**c–e**). Osteolysis and sequester formation is evident. Follow-up CT scan 7 months after renewed surgical revision (**f**). The osteolytic bone defects have been filled with lyophilized cartilage, which is showing a beginning sclerosis

12.3 Secondary Chronic Osteomyelitis: Case Reports

12.3.6 Case Report N° 10

Secondary Chronic Osteomyelitis Associated with Bone Pathology

Case Report N° 10 – Summary	
Diagnosis	Secondary chronic osteomyelitis associated with bone pathology
Affected bone	Anterior mandible
Patient	78-year-old woman
General medical history	Breast cancer with multiple lytic skeletal metastases for years; patient treated with pamidronat (Aredia, Novartis Pharma Schweiz, Bern) for the past 3 years
Dental/maxillofacial-related medical history	Since 8 months persisting chronic pain in the anterior mandible with strong periodontal disease; positive history for sequester and pus formation
Clinical symptoms	Multiple fistula formation with pus Increased mobility of the teeth (grades II–IV)
Treatment	Cessation of pamidronat (Aredia, Novartis Pharma Schweiz, Bern) Antibiotic therapy Initial major surgical debridement Revision surgical debridement Dental implants and prosthetic rehabilitation

A 78-year-old woman was referred by her dentist for evaluation and treatment of severe periodontal disease with abscess formation involving the anterior teeth in the mandible. The patient experienced recurrent pain in the right and anterior mandible for approximately 8 months and started having recurrent pus discharge and small pieces of bone from her gum. Her general medical history revealed breast cancer with skeletal metastasis, which has been successfully treated for the past 3 years with pamidronat (Aredia, Novartis Pharma Schweiz, Bern).

At initial presentation oral examination showed massive active periodontal disease of the remaining teeth in the lower jaw with multiple fistula and pus discharge from the gingival sulci (Fig. 12.10a,b). All teeth, especially the incisors, demonstrated increased mobility (grades II–IV). Orthopantomography of the patient at initial presentation showed some apical radiolucencies in the incisors and canine region (Fig. 12.10c). Corresponding CT scans revealed signs of secondary chronic osteomyelitis of the mandible with a lingual periosteal reaction, osteolysis/sclerosis, and cortical irregularities in the anterior and right mandible (Fig. 12.10d–f); however, the overall bone reaction to the infection was not considered as strong as in comparable cases of secondary osteomyelitis of the mandible with no further compromise and was interpreted as a result of jeopardized bone metabolism caused by bisphosphonate therapy.

In agreement with the patient's oncologist bisphosphonate therapy was ceased. Surgical debridement was performed with extraction of all remaining teeth in the lower jaw (Fig. 12.10g). Concomitant high-dose, long-term (3 months) antibiotic treatment with clindamycin was initiated. Biopsy specimens harvested from the surgical debridement confirmed a bone infection as well as bone necrosis concordantly with secondary chronic osteomyelitis and bisphosphonate-related bone necrosis (BRON; Fig. 12.10h,i).

Despite these therapeutic efforts, chronic infection did not subside and a second, more aggressive surgical debridement was necessary after 3 months with complete removal of the entire interforaminal alveolar bone (Fig. 12.10j). Antibiotic therapy was extended to a total of 5 months.

After a follow-up of 9 months with no remaining clinical and radiological sign of remaining infection, dental implants were inserted to enable prosthetic re-

habilitation (Fig. 12.10k,l). Due to the bisphosphonate therapy, a conservative loading protocol was chosen and the implants remained submerged for 6 months. All implants demonstrated sufficient osseointegration. The soft tissue around the centrally placed dental implant, however, remained dehiscent in the entire postoperative course but did not affect the stability of the exposed implant (Fig. 12.10m). The 1-year follow-up after finish of the prosthodontic work shows a clinical and radiological stable situation with no sign of infection (Fig. 12.10n,o).





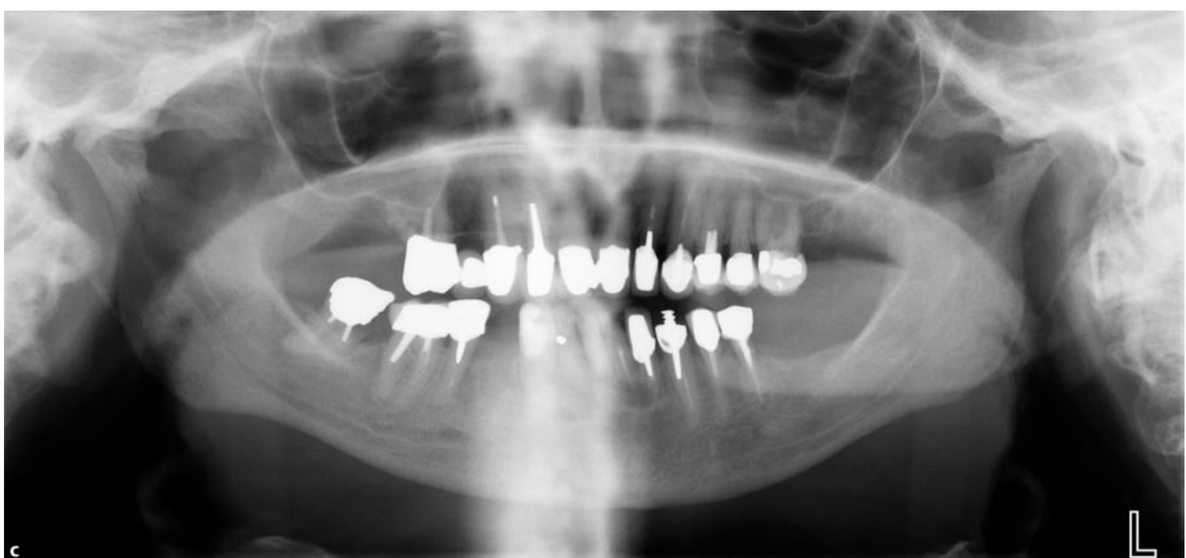
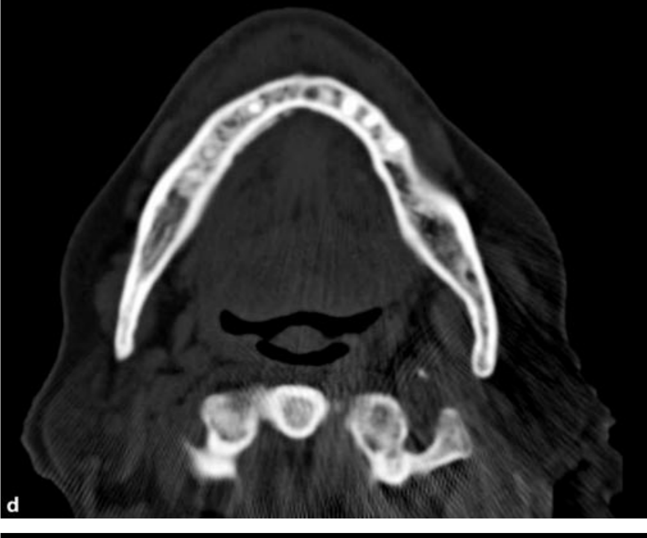
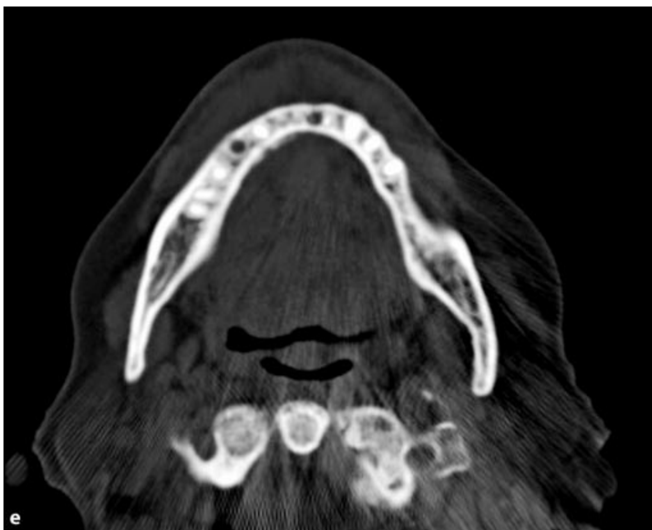


Fig. 12.10a–o Intraoral examination of the patient at initial presentation (**a,b**). Note the fistula formation and suppuration in the region of the lower left canine and from the alveolus of the shortly extracted first left premolar as well as pus arising from the gingival sulci of the incisors. Orthopantomography of the patient at initial presentation (**c**). Some apical radiolucencies are noted in the incisors and canine region. **d–o** *see next page*





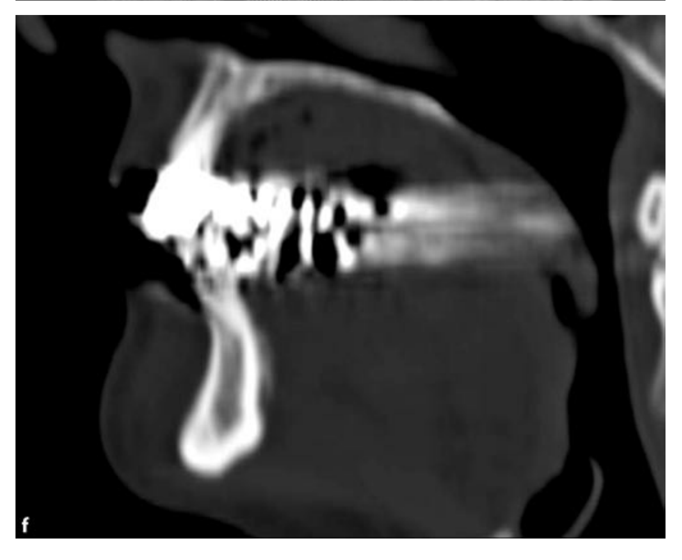


Fig. 12.10a–o (*continued*) The CT scans of the patient at initial presentation (**d–f**). The axial scans (**d,e**) clearly demonstrate a strong periosteal reaction of the right lingual cortex, some osteolysis/sclerosis, and irregularities of the cortical bone in the anterior and right mandible. The corresponding sagittal scan (**f**). The overall bone reaction is, however, not considered as strong as in comparable cases of secondary osteomyelitis of the mandible with no underlying bone pathology. **g–o** *see next page*

■ **Fig. 12.10a–o** (*continued*) Postoperative orthopantomography after extraction of the front teeth and local surgical debridement (**g**). Bone specimen harvested from the first surgical debridement (**h**). The specimen demonstrates signs of chronic osteomyelitis with lymphocytes and plasma cells; hematoxylin and eosin stain; Courtesy of R. Flury). Bone specimen harvested from the first surgical debridement (**i**). The specimen demonstrates signs of bone necrosis and marrow necrosis. The latter a sign of chronic inflammation; hematoxylin and eosin stain; courtesy of R. Flury). Postoperative orthopantomography after the second surgical debridement (**j**). **k–o** *see next page*

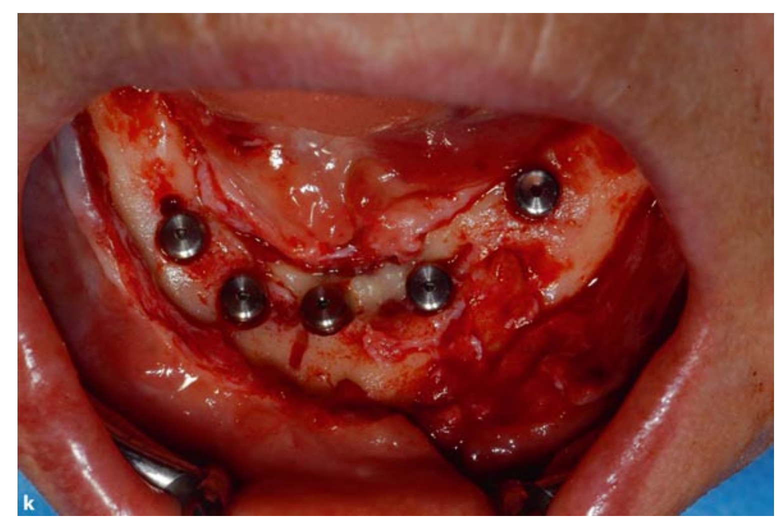




Fig. 12.10a–o (*continued*) Intraoperative view after insertion of five dental implants (**k**). Postoperative orthopantomography after placement of five dental implants (**l**). **m–o** *see next page*



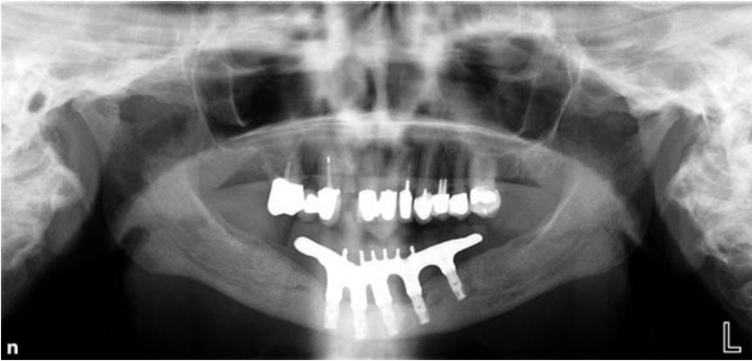




Fig. 12.10a–o (*continued*) Clinical view 6 months after insertion of dental implants (**m**). Note the persisting dehiscent alveolar mucosa due to the significantly decreased metabolism of the underlying bone which aggravates soft tissue granulation. Orthopantomography 18 months after placement of the dental implants and 1 year after completion of prosthodontic treatment (**n**). One-year follow-up after completion of prosthodontic treatment (**o**; clinical view corresponding to orthopantomography shown in **n**)

12.3 Secondary Chronic Osteomyelitis: Case Reports

12.3.7 Case Report N° 11

Case of Secondary Chronic Osteomyelitis (Not Further Classifiable)

Case Report N° 11 – Summary	
Diagnosis	Not further classifiable case of secondary chronic osteomyelitis
Affected bone	Mandibular symphysis
Patient	62-year-old man
General medical history	Cigarette smoking (>40 pack years)
Dental/maxillofacial-related medical history	Chronic skin furunculosis of the chin which eventually spread to the mandibular symphysis
Clinical symptoms	Chronic skin infection in the chin region with fistula formation and suppuration
Treatment	Antibiotic therapy Major surgical debridement and stabilization of the anterior mandible with a reconstruction plate

A 62-year-old men patient was referred to our clinic with a chronic infection of the chin region. Medical history revealed a furuncle of the chin 3 months ago which never healed. The patient is a heavy smoker with a history of more than 40 pack years. The skin infection obviously spread to deeper soft tissues and eventually to the mandibular symphysis. Initial clinical presentation showed an extraoral fistula formation with suppuration while the oral mucosa remained intact (Fig. 12.11a,b). Orthopantomography and CT scans of the mandible confirmed the diagnosis of a secondary chronic osteomyelitis of the anterior mandible (Fig. 12.11c–f). Surgical therapy consisted of an extensive debridement of the symphysis area with neurolysis of the right mental nerve (Fig. 12.11g–i). After surgical debridement, the anterior mandible was stabilized with a reconstruction plate (Fig. 12.11j). The extraoral fistula was excised with primary closure of the wound. Histopathological and microbiological assessment revealed an infection with *Actinomyces* (Fig. 12.11k). Antibiotic therapy was started as soon as specimens were harvested during surgery with clindamycin for 6 weeks. Follow-up was uneventful and clinical and radiological evaluation after 6 weeks showed no signs of persisting infection (Fig. 12.11l–r).





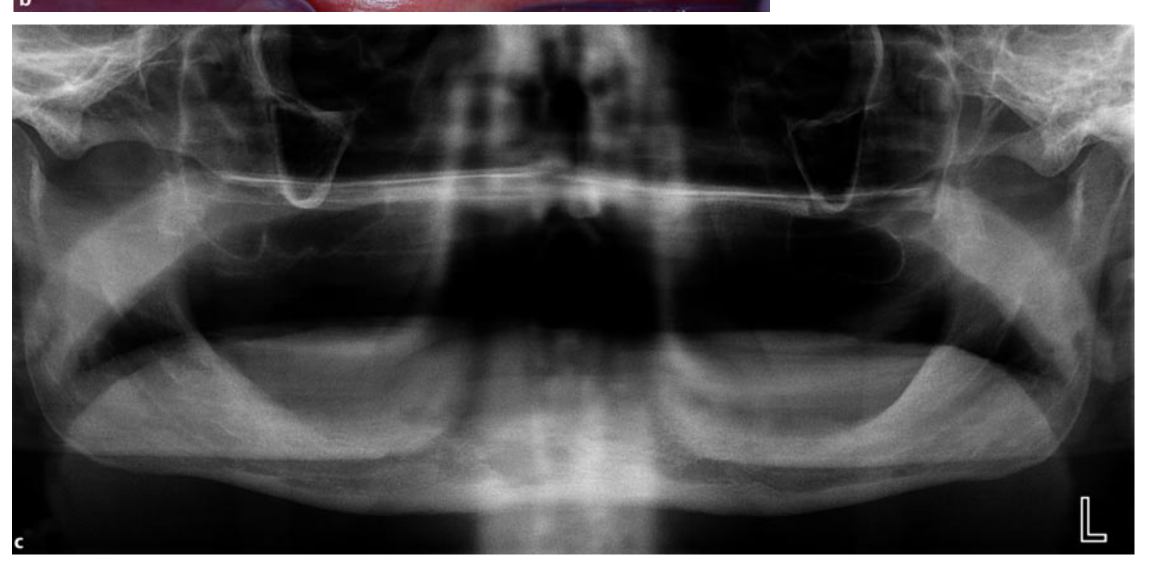


Fig. 12.11a–r Patient at initial clinical presentation demonstrates an extraoral fistula with suppuration (**a**). Patient at initial presentation (**b**). Oral view shows an edentulous mandible with an intact alveolar mucosa without any sign of fistula formation; however, a healing pressure ulcus is noted in the front vestibule. Orthopantomography of the patient at initial presentation. Note the osteolysos in the right symphysis area (**c**). **d–r** *see next page*

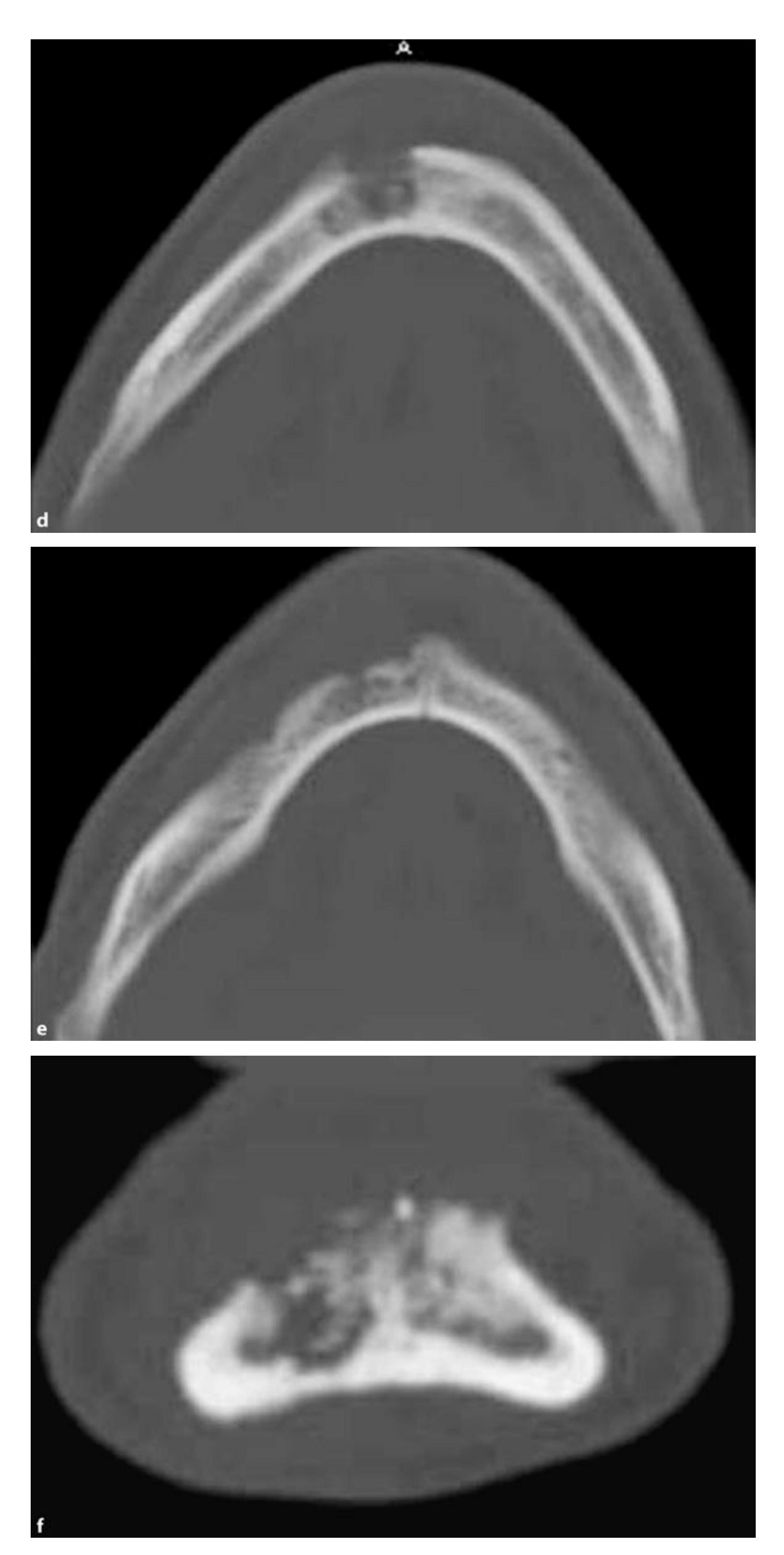


Fig. 12.11a–r (*continued*) Computed tomography scans of the patient at initial presentation (**d–f**).

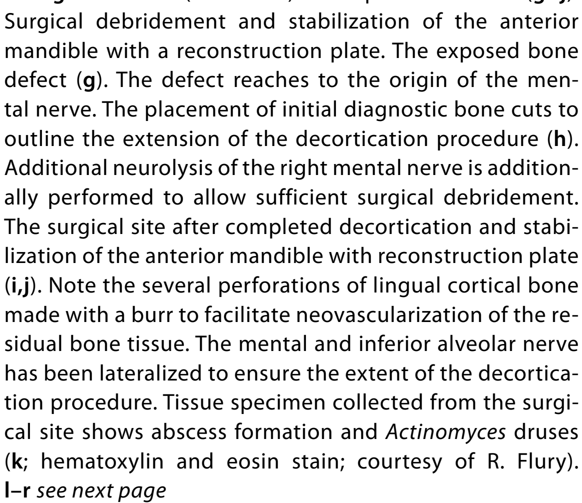


Fig. 12.11a–r (*continued*) Intraoperative views (**g–j**). Surgical debridement and stabilization of the anterior mandible with a reconstruction plate. The exposed bone defect (**g**). The defect reaches to the origin of the mental nerve. The placement of initial diagnostic bone cuts to outline the extension of the decortication procedure (**h**). Additional neurolysis of the right mental nerve is additionally performed to allow sufficient surgical debridement. The surgical site after completed decortication and stabilization of the anterior mandible with reconstruction plate (**i,j**). Note the several perforations of lingual cortical bone made with a burr to facilitate neovascularization of the residual bone tissue. The mental and inferior alveolar nerve has been lateralized to ensure the extent of the decortication procedure. Tissue specimen collected from the surgical site shows abscess formation and *Actinomyces* druses (**k**; hematoxylin and eosin stain; courtesy of R. Flury). **l–r** *see next page*





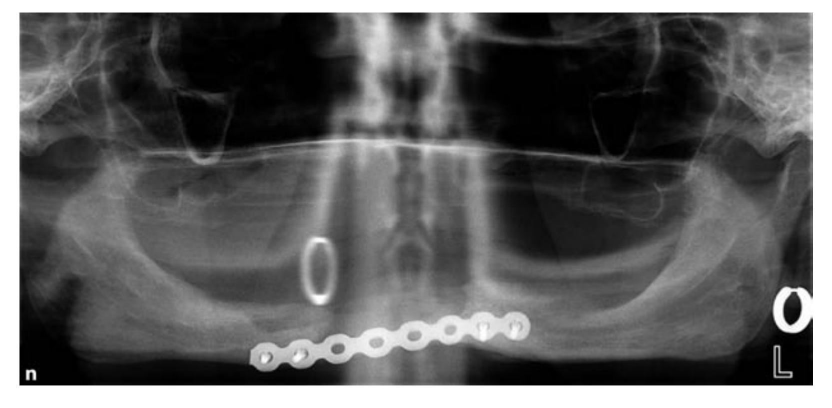


Fig. 12.11a–r (*continued*) Postoperative orthopantomography and anteroposterior view after surgical debridement and stabilization of the mandible with a reconstruction plate (**l,m**). Orthopantomography and corresponding CT scans after a 6-month follow-up (**n–p**). **o–r** *see next page*

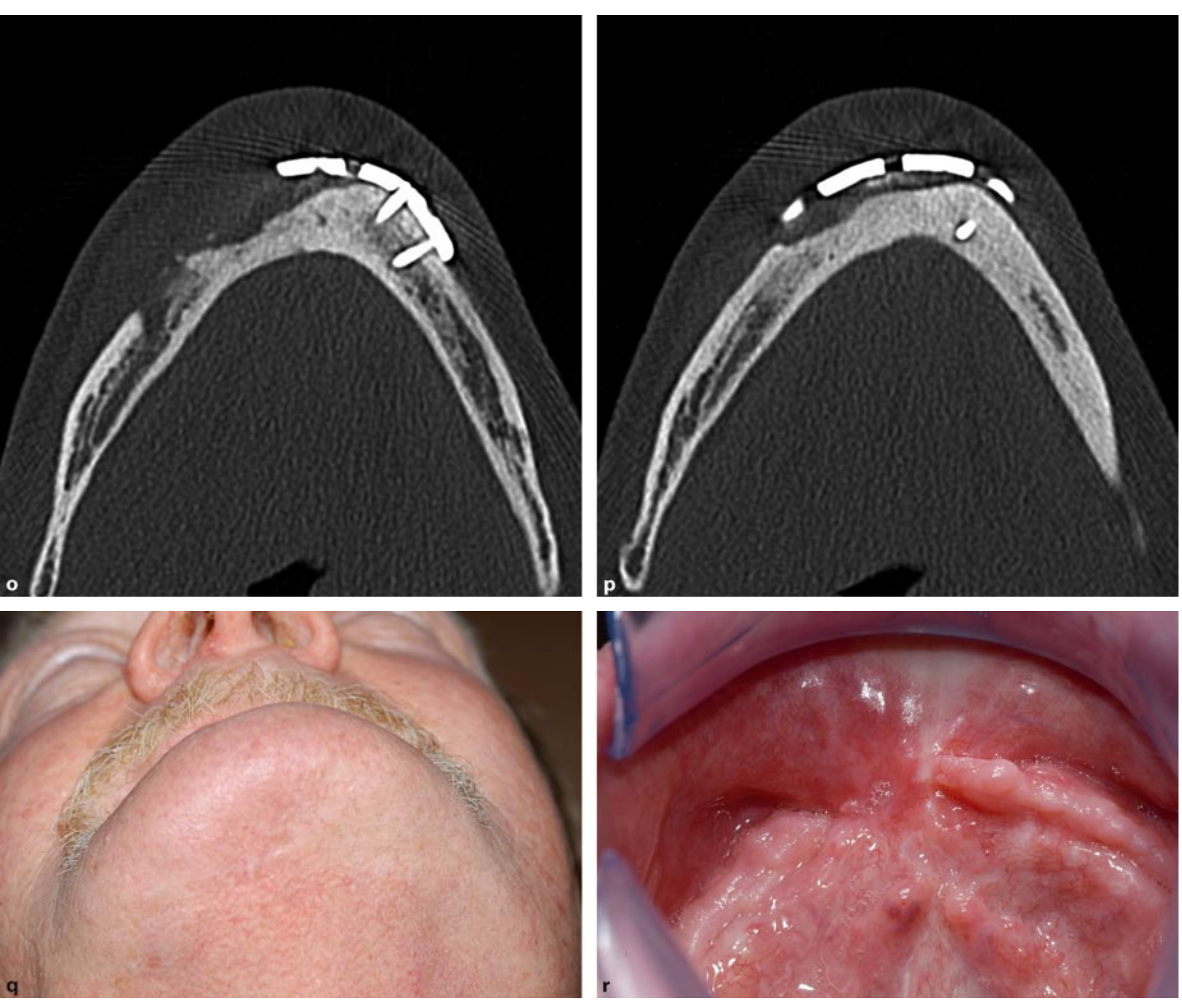


Fig. 12.11a–r (*continued*) No signs of residual infection are noted on conventional imaging. On the CT scans residual sclerosis and partial regeneration of bone can be determined. Patient 6 months after surgery (**q–r**). There is no more sign of extraoral or oral fistula formation. A small submental scar remains at the site where the fistula was excised

12.3 Secondary Chronic Osteomyelitis: Case Reports

12.3.8 Case Report N° 12

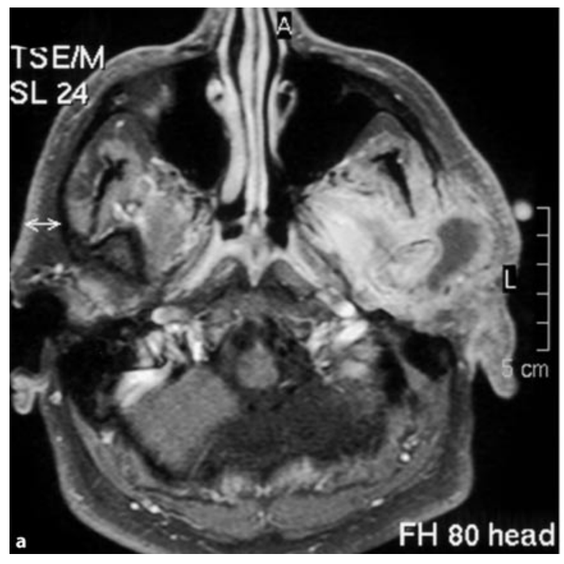
Case of Secondary Chronic Osteomyelitis (Not Further Classifiable): Solitary Secondary Chronic Osteomyelitis of the Mandibular Condyle

Case Report N° 12 – Summary	
Diagnosis	Not further classifiable case of secondary chronic osteomyelitis: solitary secondary chronic osteomyelitis of the mandibular condyle
Affected bone	Left condyle
Patient	56-year-old man
General medical history	Uneventful
Dental/maxillofacial-related medical history	Extraction of the left upper third molar several weeks prior to admission
Clinical symptoms	Repeated swelling of the left preauricular region Trismus with limited mouth opening
Treatment	Abscess drainage and microbiological assessment Antibiotic therapy Surgical debridement and abscess drainage and immediate reconstruction with a TMJ condylar prosthesis Hyperbaric Noxygen and antibiotic therapy Replacement of the fractured condylar prostheses and replacement by a costochondral graft Removal of the infected costochondral graft and replacement with a second TMJ condylar prosthesis

A 56-year-old man developed repeated swelling and trismus 6 weeks after extraction of the left upper third molar in local anesthesia. The symptoms were initially misinterpreted as a common disorder of the TMJ. Due to persisting symptoms, an MRI scan was obtained which showed diffuse inflammatory infiltration of the lateral pterygoid muscle and a subcutaneous abscess in the preauricular region (Fig. 12.12a). The abscess was surgically drained by the primary treating physician. Further radiological work-up consisted of an additional CT scan, which confirmed the suspicion of solitary osteomyelitis of the left mandibular condyle (Fig. 12.12b,c). The patient was referred for further treatment to the Clinic of Cranio-Maxillofacial Surgery at the University Hospital Zurich. Due to the fact that *Haemophilus aphrophilus* was isolated from the abscess, inoculation of microorganisms through the needle during enoral anesthetic injection, bacterial contamination during the tooth extraction, or a bacteremia following dental extraction were suggested to be possible causes for the infection.

Clinical examination demonstrated a painful diffuse swelling of the left check and a reduced mouth opening. The former extraction area was completely healed. No elevated temperature was noted and blood work-up revealed normal leukocyte count and CRP values.

Therapy consisted of continuation of high-dose antibiotics with amoxicillin/clavulanic acid which were already started prior to admission. The left mandibular condyle and the necrotic lateral pterygoid muscle were surgically removed and immediate reconstruction with a TMJ condylar prosthesis (temporary 3D adjustable con-



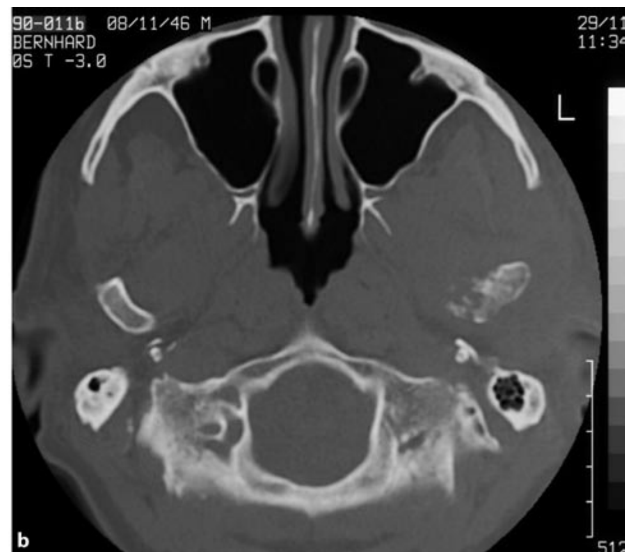




Fig. 12.12a–i An MRI scan of the patient demonstrates a diffuse inflammatory infiltration of the left lateral pterygoid muscle and a subcutaneous abscess formation in the left preauricular region (**a**). **b,c** The CT scans corresponding to the MRI scan shown in **a**: The right condyle demonstrates severe destruction with osteolysis and sequester formation, indicative for chronic osteomyelitis. **d–i** *see next page*

dylar prosthesis, System Stryker Leibinger, Stryker Leibinger, Freiburg, Germany) was performed (Fig. 12.12d).

Postoperatively, 20 sessions of HBO and further antibiotic therapy for a total of 6 weeks were conducted. Eight months postoperatively the patient was free of pain and demonstrated good function with a mouth opening of 48 mm (Fig. 12.12e).

After a 2-year period with good function, the TMJ prosthesis fractured and was replaced by a costochondral graft. Due to infection of the graft it was replaced in a subsequential surgery by a second TMJ condylar prosthesis (System Medartis; Medartis, Basel Switzerland; Fig. 12.12f,g) Postoperative HBO and long-term antibiotics were additionally administered.

The additional 2-year follow-up of the patient is, to date, uneventful with good mandibular function; however, microvascular reconstruction is being discussed as a possible procedure in the mid-term future.

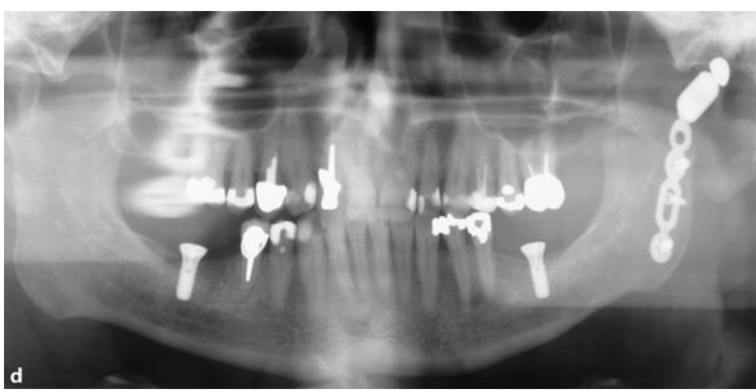
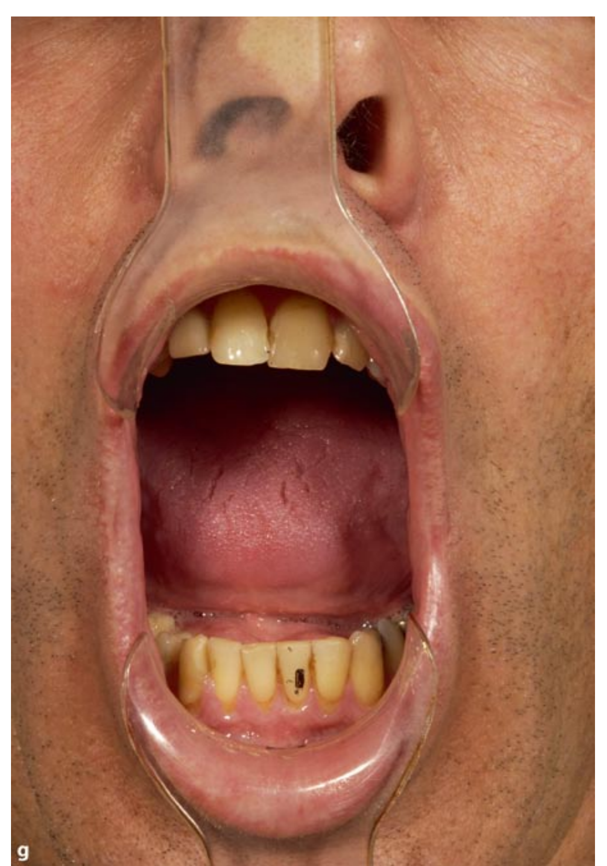






Fig. 12.12a–i (*continued*) Postoperative orthopantomography and anterior-posterior view after condylar resection and reconstruction with a condylar prosthesis (**e**,**f**). **g–i** *see next page*





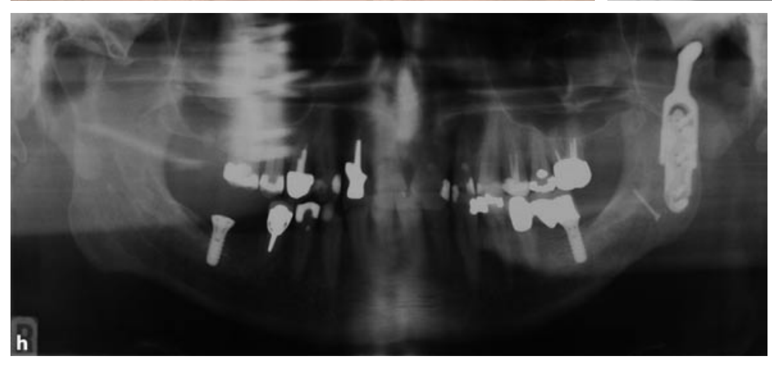


Fig. 12.12a–i (*continued*) Jaw function 8 months postoperative after condylar resection and replacement with a condylar prosthesis (**g**). An intercanthal distance of approximately 35 mm is measured with only a mild deviation of the lower jaw to the left (the *black marking* on the left lower incisor demonstrates the midline in occlusion). **h,i** Orthopantomography and anteroposterior view 4 months after removal of the infected costochondral graft and replacement by a condylar prosthesis (System Medartis; Medartis, Basel Switzerland)

12.4 Primary Chronic Osteomyelitis: Case Reports

12.4.1 Case Report N° 13

Early-onset Primary Chronic Osteomyelitis

Case Report N° 13 – Summary	
Diagnosis	Early-onset primary chronic osteomyelitis
Affected bone	Left mandible
Patient	12-year-old boy
General medical history	Uneventful
Dental/maxillofacial-related medical history	Age-related mixed dentition
Clinical symptoms	Painful swelling of the left mandible
Treatment	Repeated decortications Hyperbaric oxygen NASID Antibiotic therapy Bisphosphonates

A 12-year-old boy was referred to our clinic with painful swelling of the left mandible. Osteosarcoma or fibrous dysplasia was suspected as differential diagnosis. Initial imaging studies (orthopantomography and CT scan) showed a mixed sclerotic–lytic pattern in the affected area of the left angle and ascending ramus (Fig. 12.13a–c). Several biopsies indicated a chronic inflammation of the mandible consistent with primary chronic osteomyelitis (Fig. 12.13d–f).

Repeated decortication and extensive periosteum resection were performed. In adjunction long-term hyperbaric oxygen (60 sessions) and antibiotic therapy with clindamycin and metronidazol (24 months) were administered. Initially, a significant clinical improvement was noted. The antibiotics showed good effect while administered. Follow-up imaging studies demonstrated an almost complete recovery with restoration of bony structure (Fig. 12.13g–i). Recurring episodes two to three times a year of variable intensity have been treated thus far with short-term (4 weeks) antibiotics and NSAIDs; however, with an increasing loss of their effect. Follow-up orthopantomogram and CT images of the patient at age 17 years (5 years after onset) showed a clear relapse with a predominant lytic pattern and partial cortical destruction (Fig. 12.13j–l). Because of persisting clinical symptoms, a total of four cycles (single shot 30 mg) of pamidronate (Aredia, Novartis Pharma Schweiz, Basel) were administered over a period of 2 years, which has led to a full remission of clinical symptoms. A complete rheumatological work-up revealed no signs of extragnathic dermatoskeletal lesions, ruling at a SAPHO syndrome at this point.

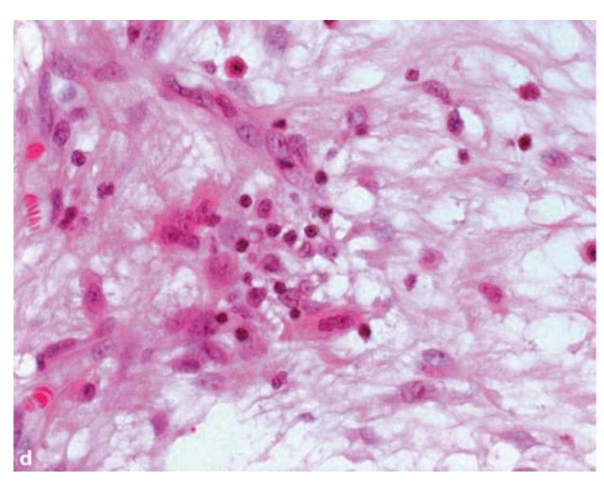
For 4 years the patient has been completely free of symptoms. In a 10-year follow-up the clinical examination revealed a contour defect of the left mandibular angle. The function of the lower jaw was unrestricted and the occlusion normal, as was the sensory function of the inferior alveolar nerve; however, the first and second left lower molar demonstrated negative vitality testing without a clinically or radiologically apparent dental pathology. Conventional and CT/MRI images demonstrate predominant sclerosis and a persisting mandibular deformity, which cannot be explained alone as a late result after repeated decortication (Fig. 12.13m–u). A region of marked osteolysis indicating possible residual activity is also persistent, as well as an incomplete pseudoarthrosis, which is explained by a 6-month-old, untreated trauma the patient sustained (Fig. 12.13p,q); however, due to the complete clinical absence of symptoms, further surgical or medical intervention is not being considered at this stage. The patient is being kept in a follow-up.

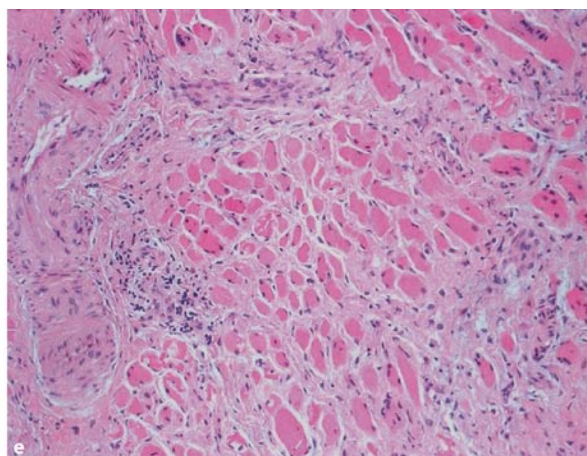






Fig. 12.13a–u Orthopantomography at initial presentation demonstrates a mixture of osteolytic and sclerosis with a strong periosteal reaction (mixed pattern) of the left mandibular angle and ascending ramus (**a**). Initial CT (axial, **b**; corresponding coronal scans, **c**) demonstrate a mixed pattern with sclerotic and radiolucent zones, extensive subperiosteal bone formation with thickening of the left mandibular angle, and dissolution of the cortical–medullary border (From Eyrich 2003). **d–u** *see next page*





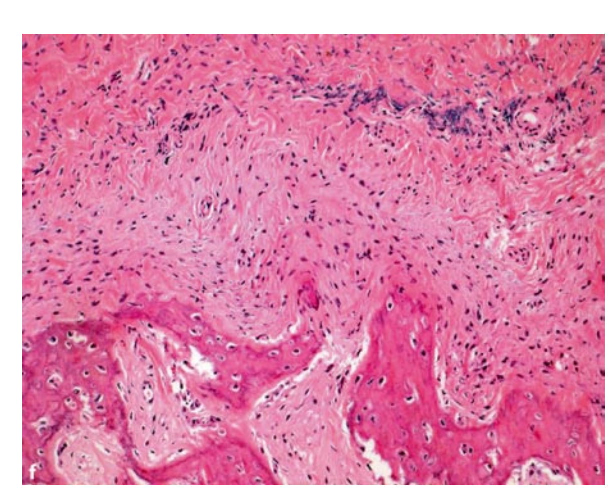
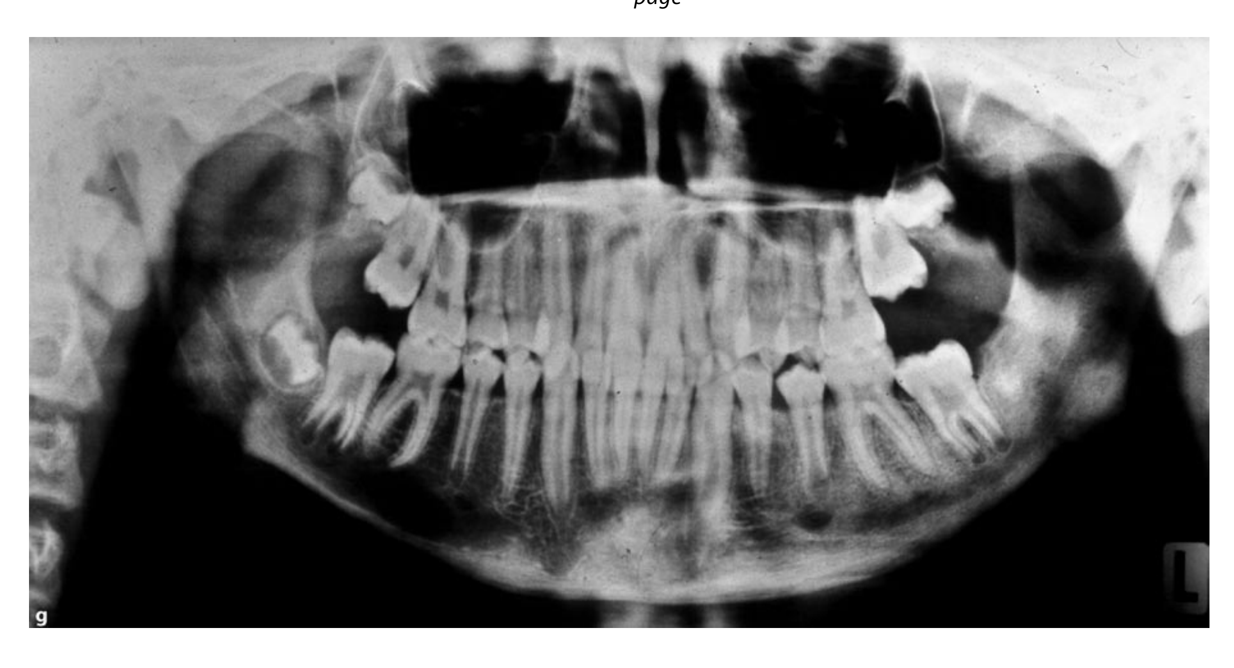


Fig. 12.13a–u (*continued*) Biopsy specimens taken at initial presentation (age 12 years) from different areas of the affected left mandibular angle and ascending ramus (**d–f**). Loose fibromyxoid tissue replaces hematopoetic bone marrow and shows a cluster of lymphoid cells as a sign of chronic inflammation (**d**; hematoxylin and eosin stain ×400). Extraosseous skeletal muscle with scarring, atrophy, and focal lymphoid infiltrates document involvement of the neighboring soft tissue (**e**; hematoxylin and eosin stain ×100). Periosteal reaction of immature woven bone at the bottom is shown adjacent to periosteal cambium layer and extraosseous fibrous collagenous tissue at the top (**f**). In this soft tissue, scattered inflammatory cells are visible (hematoxylin and eosin stain ×100). Follow-up orthopantomography 2 years after surgical, long-term antibiotic and hyperbaric oxygen treatment reveals significant recovery with restoration of bony architecture of the left mandibular angle and ascending ramus. **h–u** *see next page*



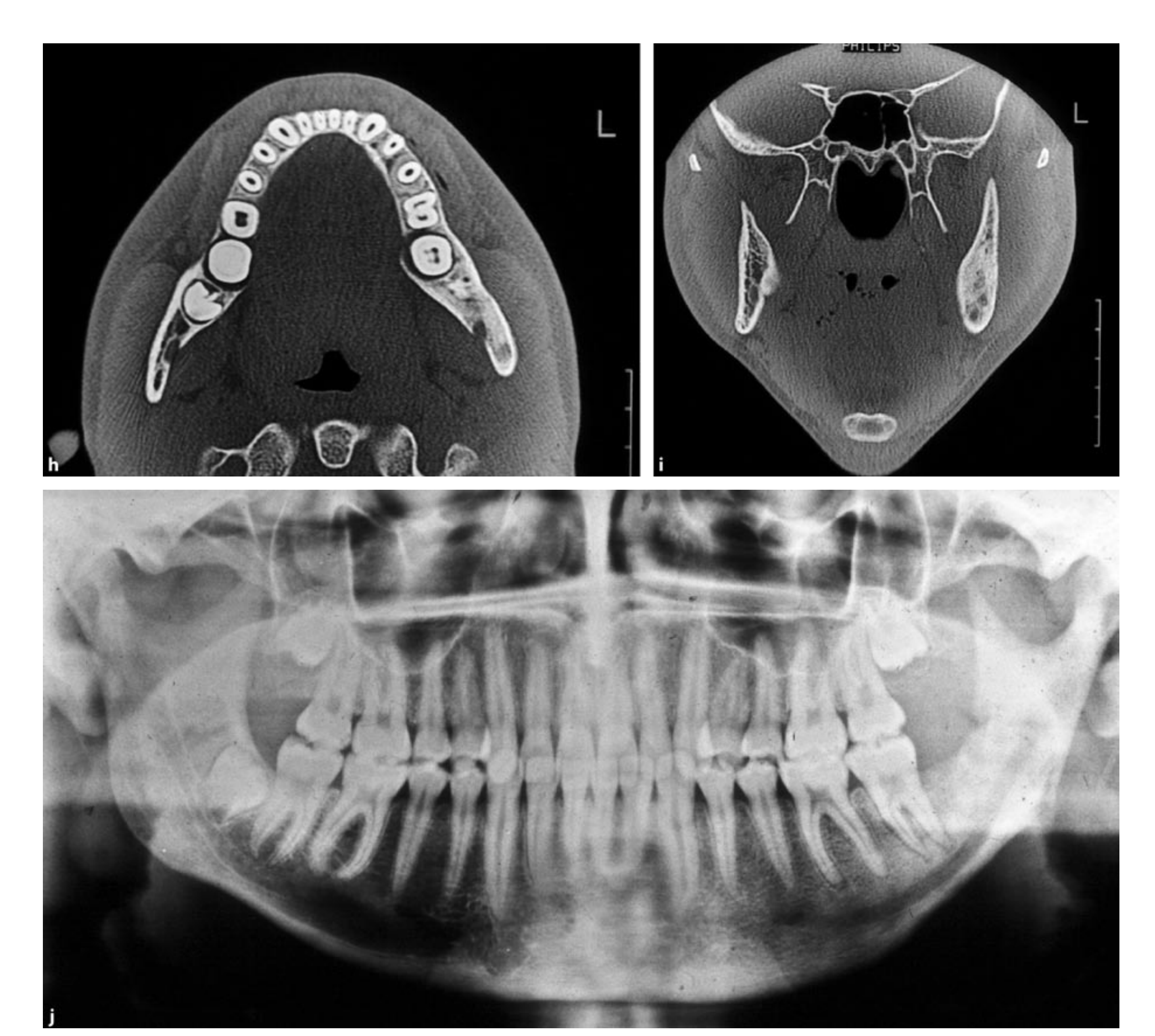


Fig. 12.13a–u (*continued*) Follow-up CT (**h**) and corresponding coronal scan (**i**) 2 years after treatment reveals a significant recovery with restoration of bony architecture on the left side. Orthopantomography of the patient at age 17 years (5 years after onset of disease) shows a relapse with again extensive osteolysis and some sclerosis (**j**). The outer cortical border has been removed in the meantime in another surgical decortication procedure. **k–u** *see next page*

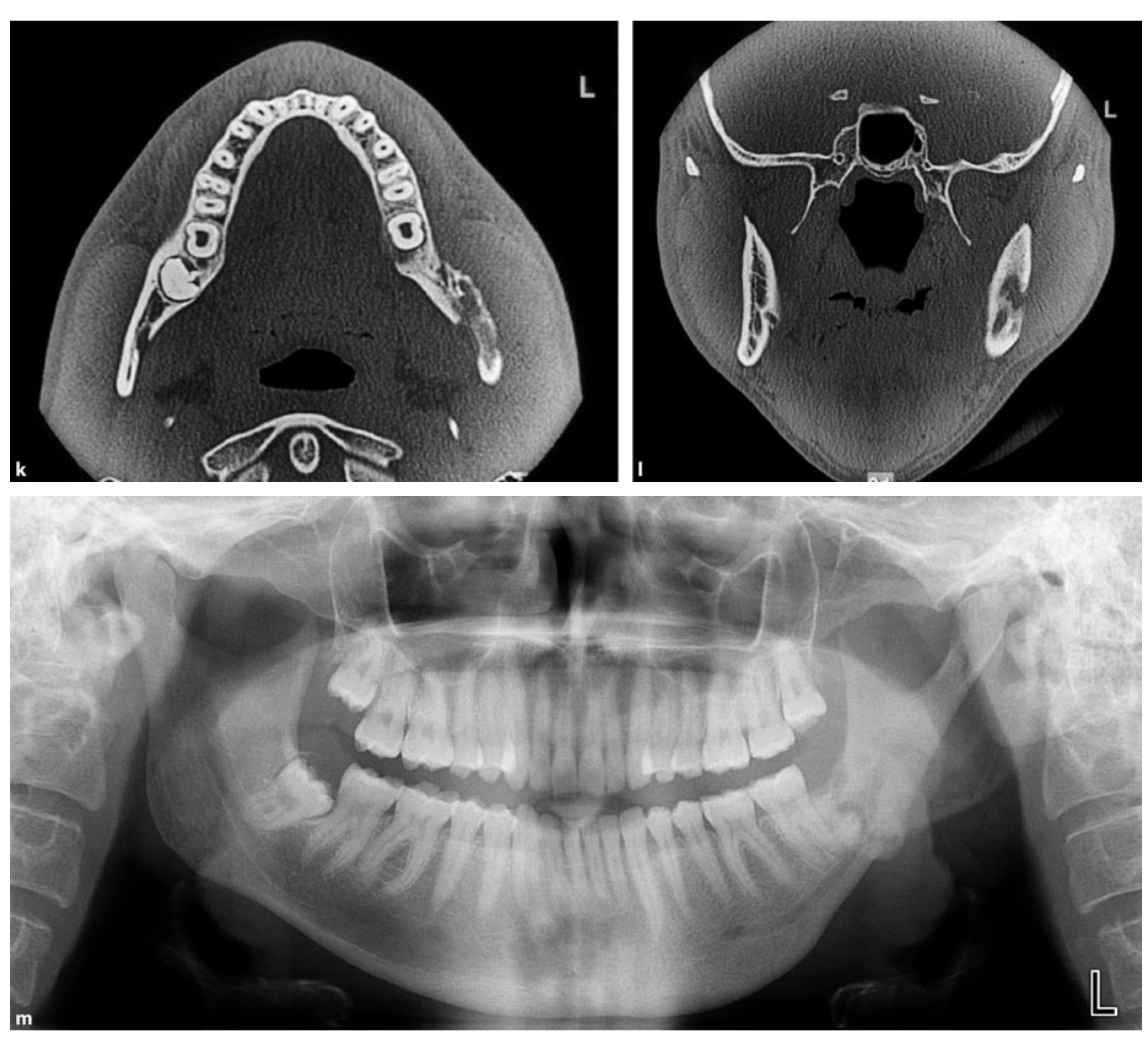


Fig. 12.13a–u (*continued*) Corresponding axial (**k**) and coronal CT scans (**l**) to orthopantomography shown in **j** demonstrates a relapse on the left side (from Eyrich 2003). **m,n** The 10-year follow-up: orthopantomography (**m**) and anteroposterior view (**n**). **n–u** *see next page*

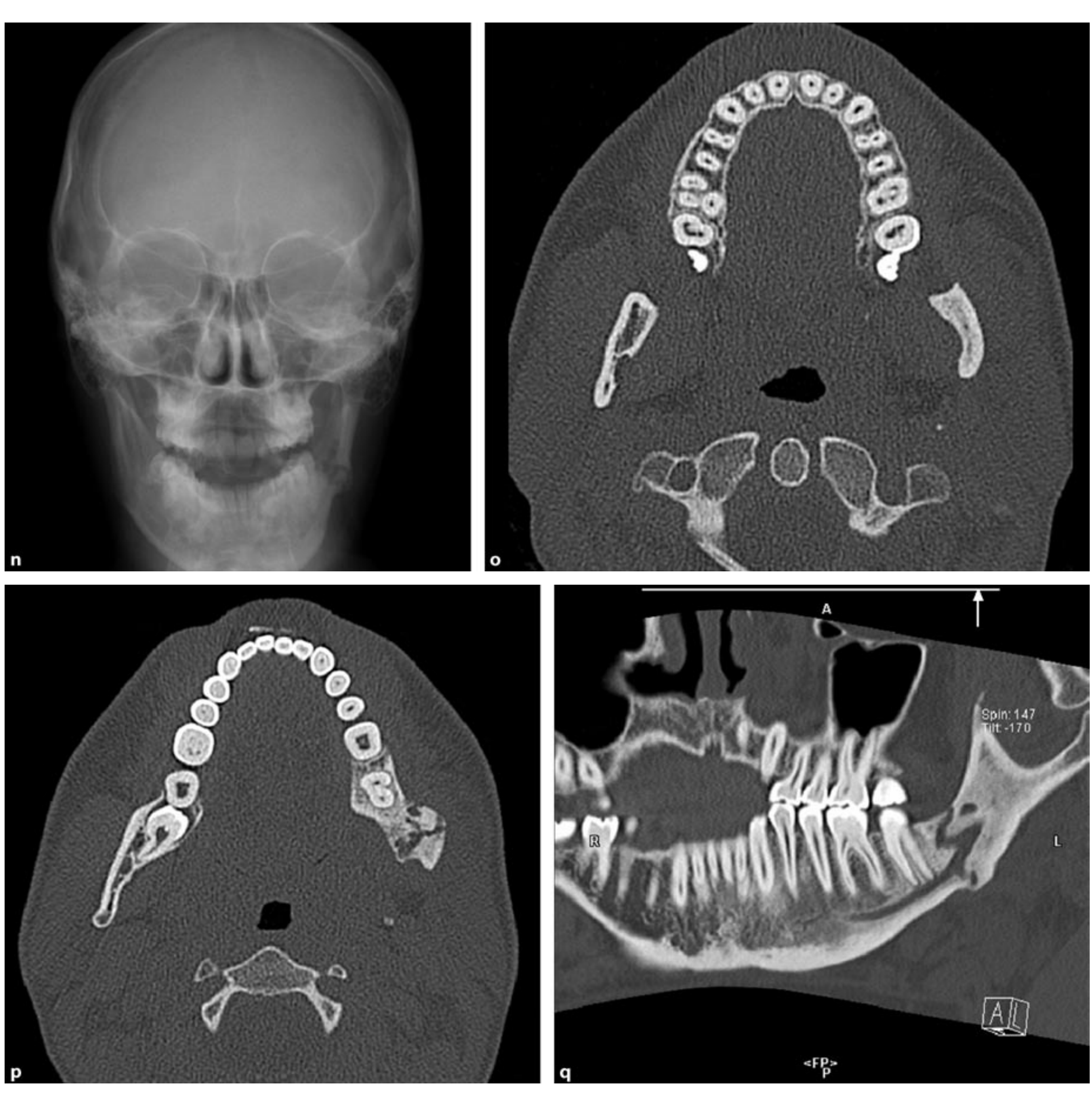


Fig. 12.13a–u (*continued*) **o–u** The 10-year follow-up CT and MR images: CT scans demonstrate residual increased sclerosis of the left mandibular angle and ascending ramus compared with the unaffected right mandible (**o–q**). There is an interruption of the contour in the mandibular angle representing an incomplete pseudoarthrosis (**p,q**). No radiological signs of active disease (e.g., osteolysis/periosteal reaction) are noted. **r–u** *see next page*



■ **Fig. 12.13a–u** (*continued*) The corresponding T1 weighted MR image at the level of the ascending ramus and upper jaw (**r**), at the level of the mandibular angle (**p**) and at the corresponding axial T2 weighted image (**t**) depict decreased signal and an increase in size of the angle of the mandible on the left. The coronal T1 image (**u**) shows a foreshortened left ascending ramus and extension of low signal corresponding to sclerosis into the coronoid process

14.4.2 CASE REPORT N° 14

Adult-onset Primary Chronic Osteomyelitis

Case Report N° 14 – Summary	
Diagnosis	Adult-onset primary chronic osteomyelitis
Affected bone	Left mandibular corpus
Patient	51-year-old man
General medical history	Alcohol abuse Cigarette smoking (> 40 pack years) Hypertension
Dental/maxillofacial-related medical history	General periodontal disease with extraction of the remaining left lower second molar 18 months prior to presentation Already symptoms of recurrent swelling of the left mandible 10 years ago
Clinical symptoms	Recurrent pain and swelling of the left mandibular region Regional lymphadenopathy (level-I left)
Treatment	Hyperbaric oxygen Neurolysis of the inferior alveolar nerve, partial resection of the left mandible, and immediate reconstruction with autologous bone from the iliac crest Short-term postoperative antibiotic therapy (clindamycin)

A 51-year-old man presented with a history of recurrent pain and swelling of the left mandibular region for 6 months. Extraction of a remaining left molar with periodontal damage 18 months prior showed no improvement, however. The patient had experienced similar symptoms with swelling of the left mandible 10 years prior but did not seek medical attention because of spontaneous clinical remission of symptoms. His general medical history revealed alcohol abuse and strong cigarette smoking as well as hypertension. Initial clinical presentation showed swelling of the left mandible and surrounding soft tissue with mild pain on palpation (Fig. 12.14a,b). Furthermore, enlargement of submandibular lymph nodes level I on the left side was noted. Dental examination showed moderate to severe periodontal disease with generalized loss of attachment.

Conventional and CT imaging revealed a diffuse sclerosis of the entire left mandible and the symphyseal region (Fig. 12.14c–g). Scintigraphy demonstrated an increased uptake of the affected left mandible. A further minor increase in activity in the knee joints was consistent with beginning gonarthrosis (Fig. 12.14h). Due to the patient's history, as well as clinical and radiological findings, the diagnosis of primary chronic osteomyelitis of the left mandible was made. A bone biopsy was made to further support the diagnosis, which showed signs of chronic bone infection (Fig. 12.14i,j); however, microbiological examination of the bone specimen showed no growth of bacteria.

Preoperative HBO therapy (20 sessions) was conducted followed by partial resection of the left mandible with immediate reconstruction with autologous bone from the iliac crest and neurolysis of the inferior alveolar nerve. The also affected condyle was left in place (Fig.12. 14k,l). Postoperative short-term antibiotics (clindamycin) were administered. The further course was uneventful. Ten months later, the reconstruction plate was removed upon the patient's request. Intraoperative inspection demonstrated good local vascularization and vitality of the transplant and adjacent bone tissue. Orthopantomography showed good transplant survival (Fig. 12.14m).In the subsequent 2.5 years no sign of relapse has been noted thus far.

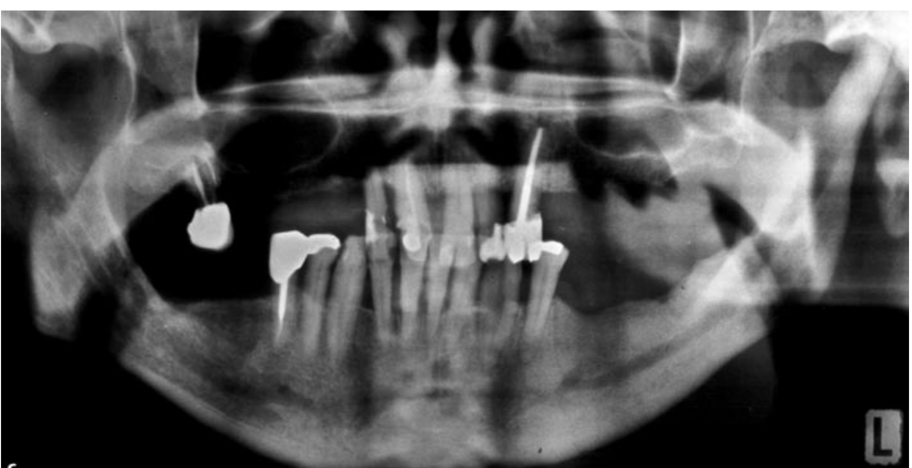
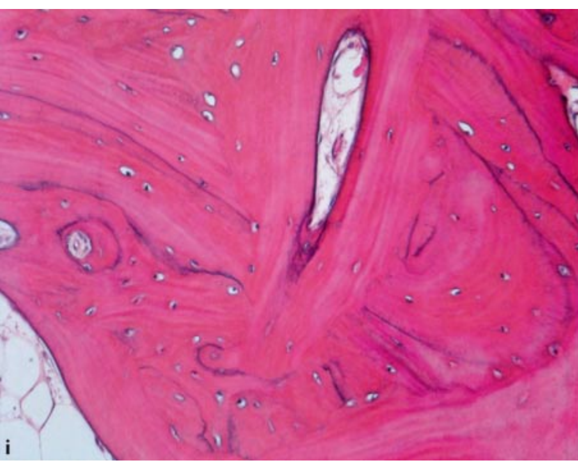
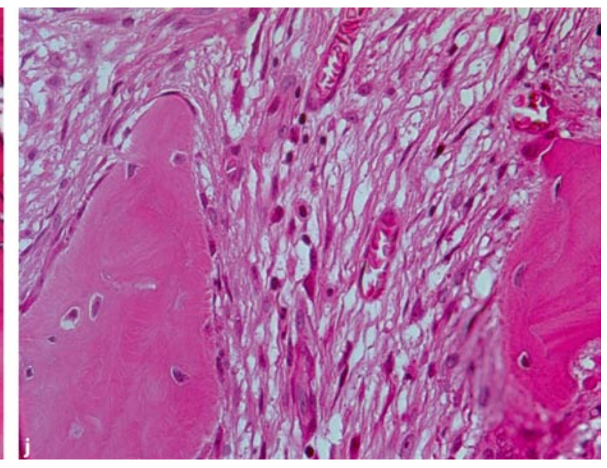


Fig. 12.14a–m Frontal (**a**) and lateral (**b**) view of the patient at the beginning of an active episode with predominant unilateral swelling of the left lower mandibular angle (from Baltensperger et al. 2004). Orthopantomography at initial presentation demonstrating diffuse sclerosis of the entire left mandible from the condyle to the symphyseal region (**c**). (From Baltensperger et al. 2004) **d–m** *see next page*



Fig. 12.14a–m (*continued*) Coronal and axial CT scans of the mandible demonstrate the diffuse sclerotic bone pattern with grossly dissolved cortical–medullary borders (**d–g**). The sclerosis is predominantly enossal with minimal enlargement of the left mandibular bone. Note the surrounding sclerosis that demarcates the mandibular canal and the partial destruction of the left condyle surface compared with the right side (from Baltensperger et al. 2004). Scintigraphy at initial presentation demonstrates increased uptake of the affected left mandible (**h**). Increased uptake in both knee joints is consistent with a positive history of moderate gonarthrosis. No other bone or joint involvement is noted. **i–m** *see next page*

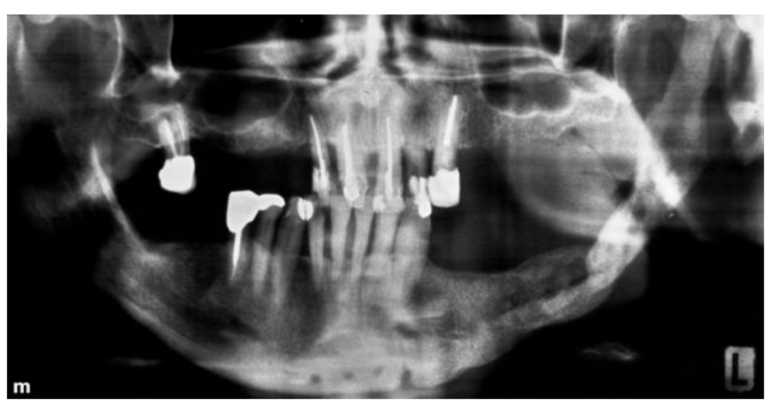



Fig. 12.14a–m (*continued*) Biopsy specimen (**i**): Paget-like bone formation with irregular reversal lines (hematoxylin and eosin ×10). Biopsy specimen (**j**): medullar fibrosis (hematoxylin and eosin ×50). Intraoperative view (**k**): the resected mandible has been reconstructed with autologous bone taken from the iliac crest. Orthopantomography taken after partial resection of the left mandibular corpus and immediate reconstruction with autologous bone from the iliac crest and a 2.4-mm reconstruction plate (**l**). Orthopantomography 10 months postoperative, after partial resection with immediate reconstruction (**m**): The reconstruction plate has been removed. The transplant shows a normal bone structure. There is no radiological evidence of a relapse

12.4 PRIMARY CHRONIC OSTEOMYELITIS: CASE REPORTS

12.4.3 CASE REPORT N° 15

Adult-onset/Syndrome-associated Primary Chronic Osteomyelitis

Case Report N° 15 – Summary	
Diagnosis	Adult-onset/syndrome-associated primary chronic osteomyelitis
Affected bone	Left and part of the right mandible
Patient	66-year-old man
General medical history	History of cigarette smoking COPD Monoclonal gammopathy
Dental/maxillofacial-related medical history	Partial edentulous Periodontal disease with loss of attachment
Clinical symptoms	Recurrent episodes of pain and selling of the right mandible Palmoplantar pustulosis Destruction of the sterno-clavicular joint
Treatment	Hyperbaric oxygen Antibiotic therapy NSAID

A 66-year-old man presented with a 10-month history of recurrent self-limiting painful swelling of the right mandibular region. Initial orthopantomography and CT scans revealed diffuse scleroses of the entire right and part of the left mandibular body with deformation of the right mandibular body/angle (Fig. 12.15a–i). Based on the clinical picture and radiological findings, primary chronic osteomyelitis was diagnosed. Further rheumatological work-up revealed active severe destruction of the left sterno-clavicular joint (Fig. 12.15j–l). Skin symptoms consisted of mild acne and palmoplantar pustulosis (Fig. 12.15m,n). These findings together with the primary chronic osteomyelitis of the mandible were interpreted as part of a SAPHO syndrome.

Therapy with HBO (15 sessions) and antibiotics with clindamycin for 3 months were administered with partial remission of symptoms while administered. Partial mandibular resection and immediate reconstruction with autologous bone was further suggested, but the patient refused surgical treatment.

Currently, the patient still suffers periods of acute exacerbation with perimandibular pain and swelling, which are effectively treated with NSAIDs and antibiotics.



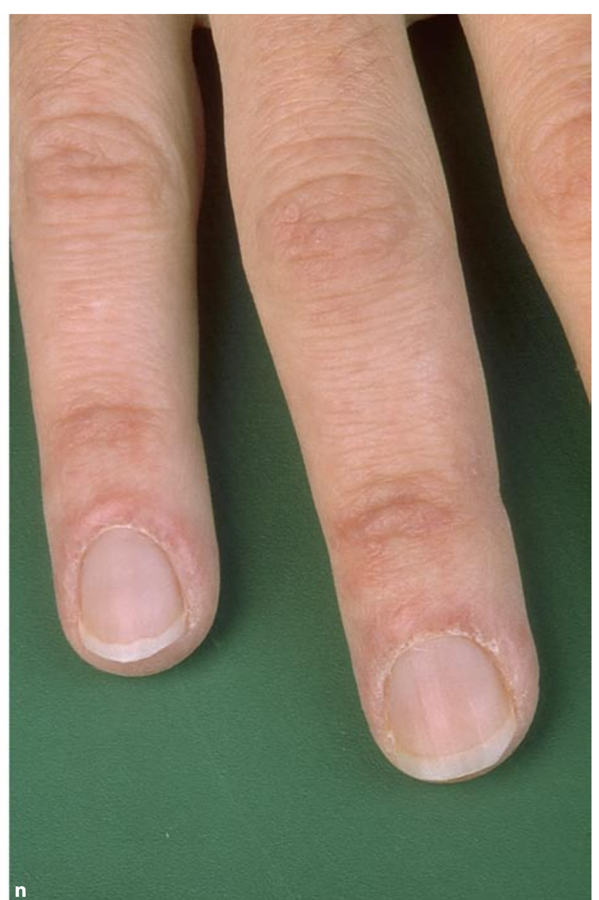
Fig. 12.15a–n An OPG shows typical sclerosis involving cortical and cancellous bone of the entire right mandibular body up to the temporomandibular joint and part of the left mandibular body (**a**). The lower left second incisor shows a periapical radiolucency and interdental vertical loss of bone due to chronic periodontal infection.

Fig. 12.15a–n (*continued*) Axial and coronal CT scans of the temporomandibular joint reveal osteolytic and cystic destruction of the right condylar head (**b–f**). **f–n** *see next page*



Fig. 12.15a–n (*continued*) Axial and corresponding CT scans of the molar region show sclerotic changes (**g,h**). The lateral aspect of the 3D reconstructed mandible shows deformation of the right mandibular body and condyle (**i**; 3D reconstruction performed with software package Gyroviewâ, ISG Technologies, Toronto, Canada). Scintigraphic imaging demonstrates a significant enhancement of the right mandibular body and the left sterno-clavicular joint (**j**). Axial CT scan of the chest wall and the sterno-clavicular joints (**k,l**). **l–n** *see next page*





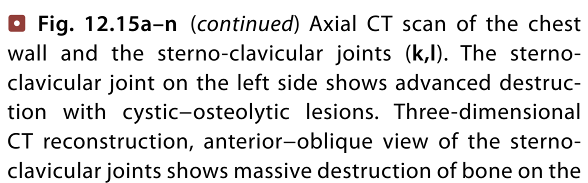


Fig. 12.15a–n (*continued*) Axial CT scan of the chest wall and the sterno-clavicular joints (**k,l**). The sterno-clavicular joint on the left side shows advanced destruction with cystic–osteolytic lesions. Three-dimensional CT reconstruction, anterior–oblique view of the sterno-clavicular joints shows massive destruction of bone on the left and hyperostosis on the right side (3D reconstruction performed with software package Gyroviewâ, ISG Technologies, Toronto, Canada). Typical pustulosis with local scaling after eruption of pustules on the planta pedis and in the dorsal finger (**m,n**). (Figures 12.16a–i and 12.16m,n are from Eyrich 1999)

12.4.4 CASE REPORT N° 16

Early-onset Primary Chronic Osteomyelitis

Case Report N° 16 – Summary	
Diagnosis	Early-onset primary chronic osteomyelitis
Affected bone	Left mandible
Patient	16-year-old girl
General medical history	Recurrent pain of the left knee joint
Dental/maxillofacial-related medical history	Endodontic treatment of the left lower first molar Past orthodontic therapy
Clinical symptoms	Recurrent episodes of (dull) pain Limitation of mouth opening Expansion of the left mandible and soft tissue swelling Mild hyposensitivity of the inferior alveolar nerve (Vincent's Symptom)
Treatment	Surgical decortication of the mandible Hyperbaric oxygen Antibiotic therapy

A 16-year-old girl was referred to our clinic from her family physician with pain and swelling of her left mandible and limited opening of the mouth. A more detailed history revealed that she had suffered from similar symptoms over the past year which usually resolved spontaneously. Furthermore, she also complained of recurrent pain of her left knee. Initial clinical examination revealed and asymmetry of the left mandible with a dull swelling of the surrounding soft tissue (Fig. 12.16a,b). The dental exam was uneventful except for a past endodontic treatment in her first left lower molar and a lingual retainer after orthodontic treatment she had received in the past. No sign of an active or chronic dental focus was noted (Fig. 12.16c). Suppuration and/or fistula formation were absent. A mild hyposensitivity of the inferior alveolar nerve was noticed (Vincent's Symptom). Limitation of mouth opening was observed. Cervical lymph nodes were palpable. Initial orthopantomography and anteroposterior views demonstrated an expansion of the left mandibular body causing the deformity with diffuse sclerosis (Fig. 12.16d,e). Computed tomography scans were obtained as further radiological work also determined areas of osteolysis and periosteal reaction, which was interpreted as areas of intense disease activity (Fig. 12.16f–k). Skeletal scintigraphy and PET studies were further conducted which clearly identified the left mandible as a region of disease activity (hot spot), whereas further, extragnathic skeletal manifestations of the disease were ruled out (Fig. 12.16l–o).

Initial therapy consisted of surgical decortication of the affected left mandibular corpus and angle (Fig.12. 16p–q) followed by long-term antibiotics with clindamycin for 8 months and 30 sessions of HBO. This led to a full remission of clinical symptoms.

After 2 years of complete absence of clinical activity the patient, clinical, and imaging follow-up investigation were performed. The left mandible still showed persisting deformity (Fig. 12.16r,s). Conventional imaging studies showed predominant sclerosis of the affected region (Fig. 12.16t–v). Corresponding CT scans furthermore identified areas of osteolysis (Fig. 12.16w–z); however, due to the complete absence of clinical symptoms

for more than 2 years, it was considered safe to close the persisting front open bite (Fig. 12.16t,u,zd,ze) surgically in a standard bimaxillary procedure after presurgical orthodontic therapy. Intraoperatively, a biopsy was taken from a presumably active region in the CT with marked osteolysis (white ring; Fig. 12.16 za,zb), which demonstrated predominant cortical bone with signs of remodeling, significant marrow fibrosis, and few lymphocytes and plasma cells (Fig. 12.16zc).

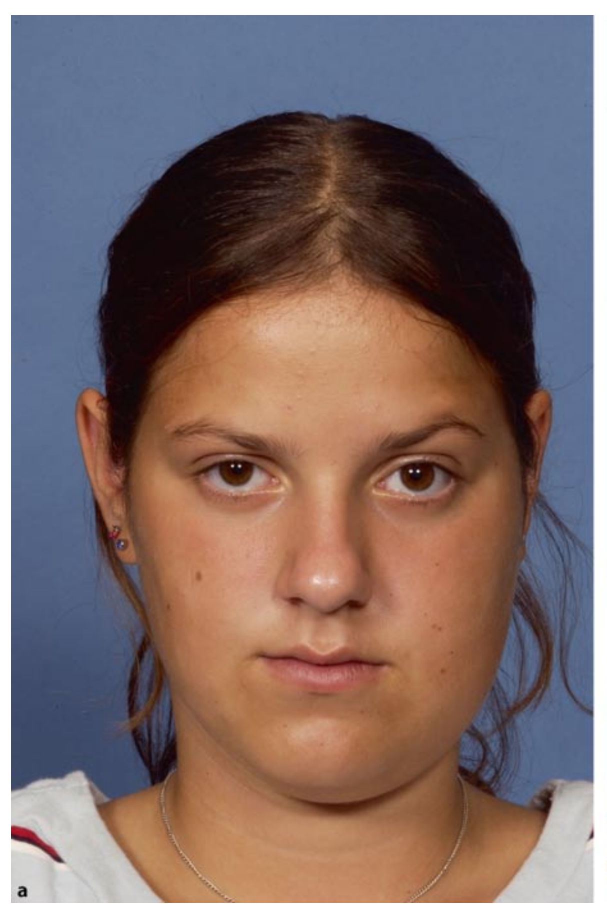






Fig. 12.16a–ze Patient at initial presentation (**a,b**): not the significant asymmetry and swelling of the left mandible and surrounding soft tissue. Dental status at initial presentation reveals no signs of an infectious focus (**c**). **d–ze** *see next page*







Fig. 12.16a–ze (*continued*) A lingual retainer has been placed after orthodontic therapy. Orthopantomography and anteroposterior view at initial presentation (**d,e**). Note the enlarged left mandible with diffuse sclerosis. Computed tomography scans at initial presentation (**f–k**). The whole left mandible is affected including the left condyle, leading to an expansive deformity of the bone. The affected area shows predominant sclerosis and areas of osteolysis which are interpreted as particularly active areas (**f,g**). **g–ze** *see next page*





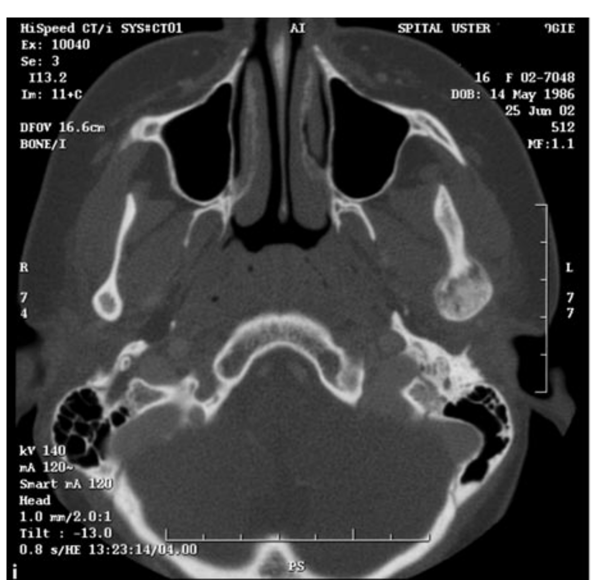
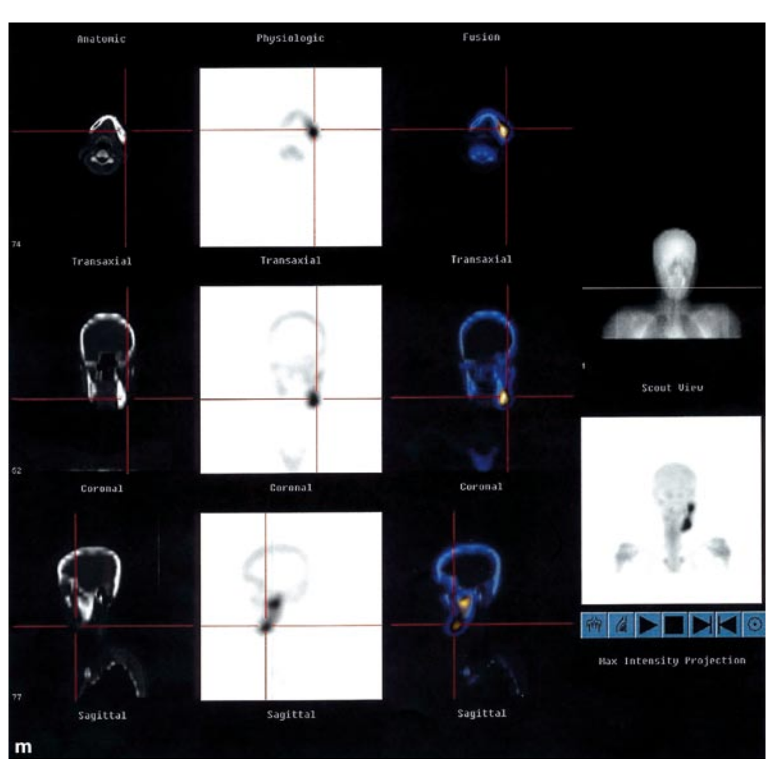




Fig. 12.16a–ze (*continued*) Note the enlarged left mandible with diffuse sclerosis. Computed tomography scans at initial presentation (**f**–**k**). The whole left mandible is affected including the left condyle, leading to an expansive deformity of the bone. The affected area shows predominant sclerosis and areas of osteolysis which are interpreted as particularly active areas (**f**,**g**). Also a strong periosteal reaction is seen, especially on the outer border of the mandibular angle and ascending ramus (**f**–**h**). **k**–**ze** *see next page*



Fig. 12.16a–ze (*continued*) Skeletal scintigraphy of the patient at initial presentation (**l**) demonstrates a significant uptake of radioactive tracer in the left mandible (hot spot); other (extragnathic) lesions are not identified. **m–ze** *see next page*



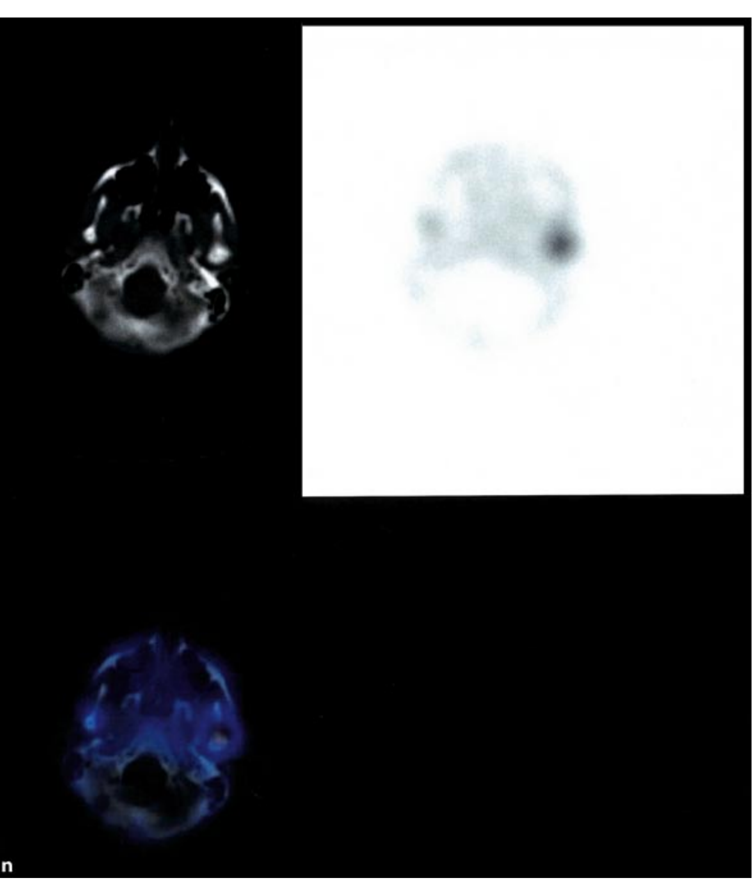


Fig. 12.16a–ze (*continued*) The PET/CT images of the patient at initial presentation demonstrate a more precise location of the active regions in the left mandible than skeletal scintigraphy (**m**–**o**). Especially two hot spots were determined: the buccal cortical area of the left mandibular angle and the left condyle. These areas corresponded with the areas of sclerosis and osteolysis (e.g., mixed pattern) and strong periosteal reaction in the CT scans shown in **f, g,** and **i.** **o**–**ze** *see next page*

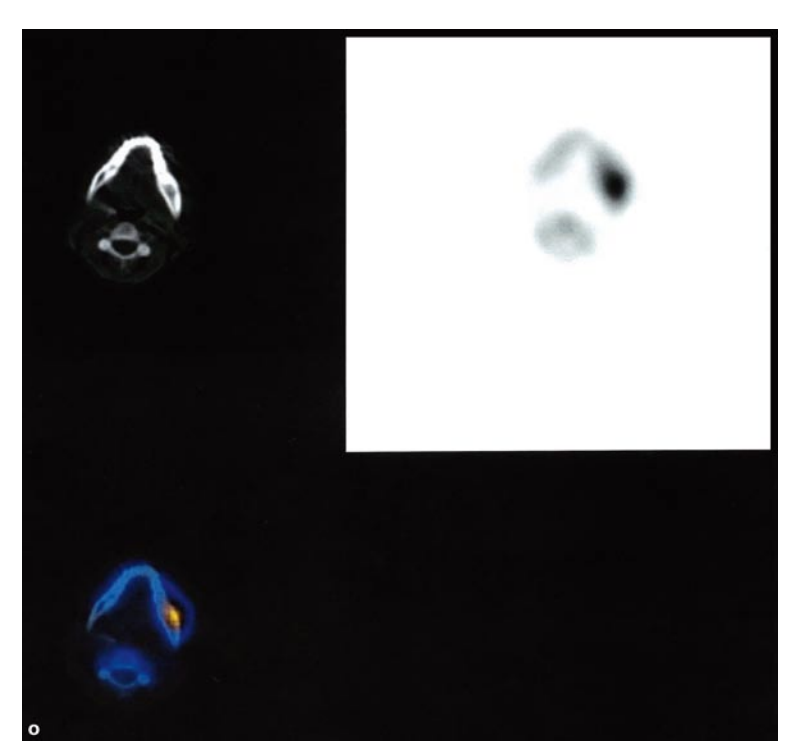


Fig. 12.16a–ze (*continued*) The PET/CT images of the patient at initial presentation demonstrate a more precise location of the active regions in the left mandible than skeletal scintigraphy (**m–o**). Especially two hot spots were determined: the buccal cortical area of the left mandibular angle and the left condyle. These areas corresponded with the areas of sclerosis and osteolysis (e.g., mixed pattern) and strong periosteal reaction in the CT scans shown in **f, g,** and **i.** **p–ze** *see next page*



Fig. 12.16a–ze (*continued*) Surgical exposition of the affected left mandible (**p**). Note that the exposed surface of the affected bone shows a distinct appearance which resembles fibrous dysplasia. Resected bone from the decortication procedure (**q**) Same patient 4 years later (**r**). Note that the deformity of the mandible is still persistent. **t–z** Imaging studies corresponding to **r** and **s**. Note the persisting asymmetry of the left mandibular corpus and angle compared with the unaffected side. **u–ze** *see next page*

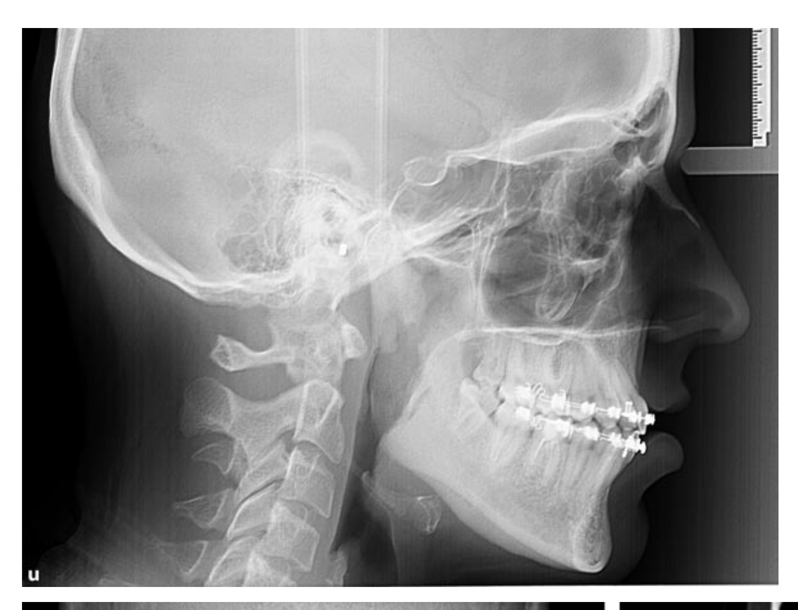


Fig. 12.16a–ze (*continued*) **t–z** Imaging studies corresponding to **r** and **s**. Note the persisting asymmetry of the left mandibular corpus and angle compared with the unaffected side. The surplus of bone of the mandibular base is especially well demonstrated in the lateral cephalogram (**u**). The corresponding CT scans still show massive sclerosis and regions of osteolysis (**w–z**). **z–ze** *see next page*

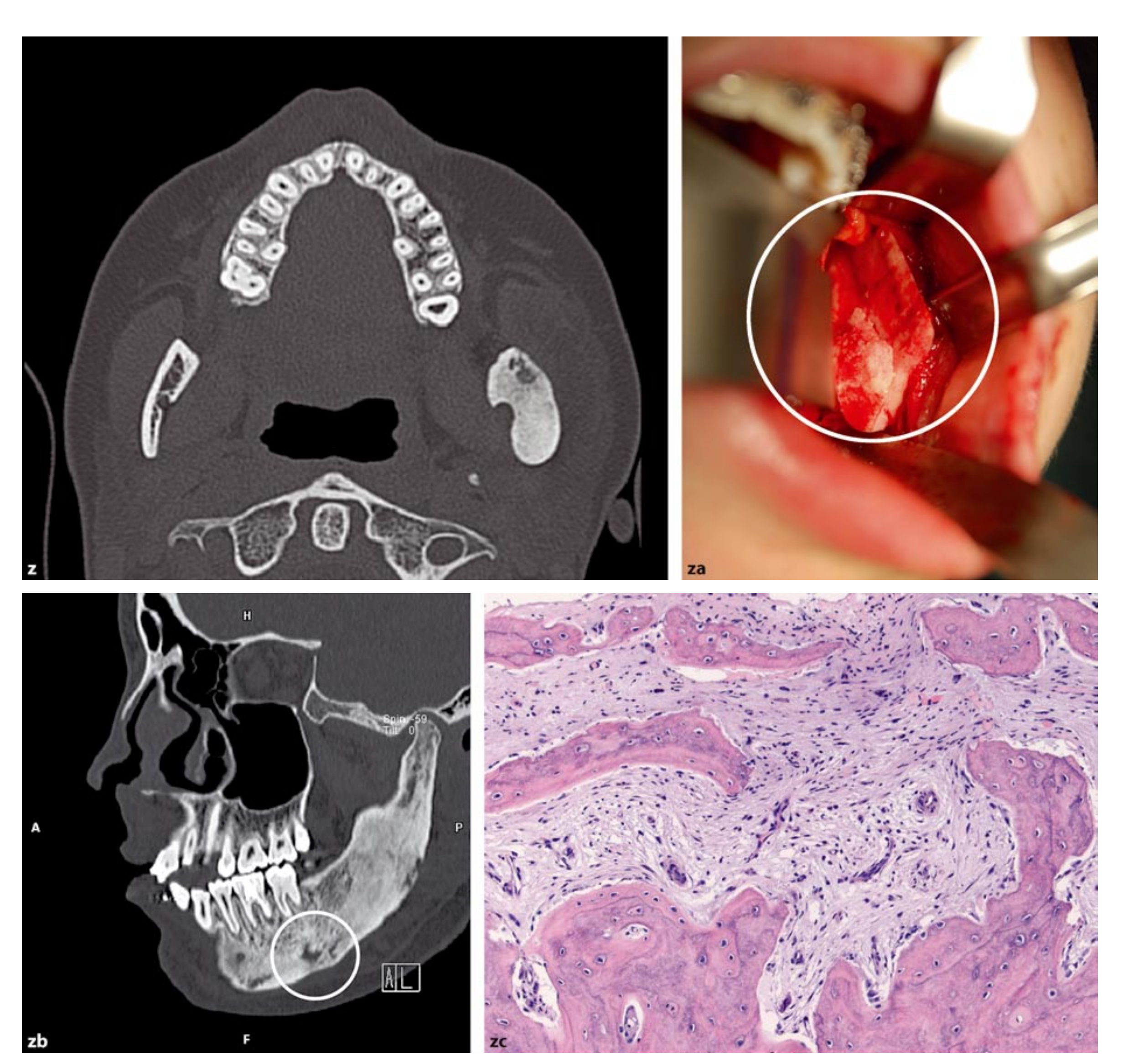


Fig. 12.16a–ze (*continued*) The corresponding CT scans still show massive sclerosis and regions of osteolysis (**w–z**). Intraoperative view during the BSSO procedure (**za**). A biopsy was taken from a region (*circle*), (**za**) which corresponds the osteolysis in the CT scan (**zb**). The histology (**zc**) shows predominant cortical bone with signs of remodeling and significant marrow fibrosis and few lymphocytes and plasma cells consistent with primary chronic osteomyelitis (hematoxylin and eosin stain). **zd–ze** *see next page*



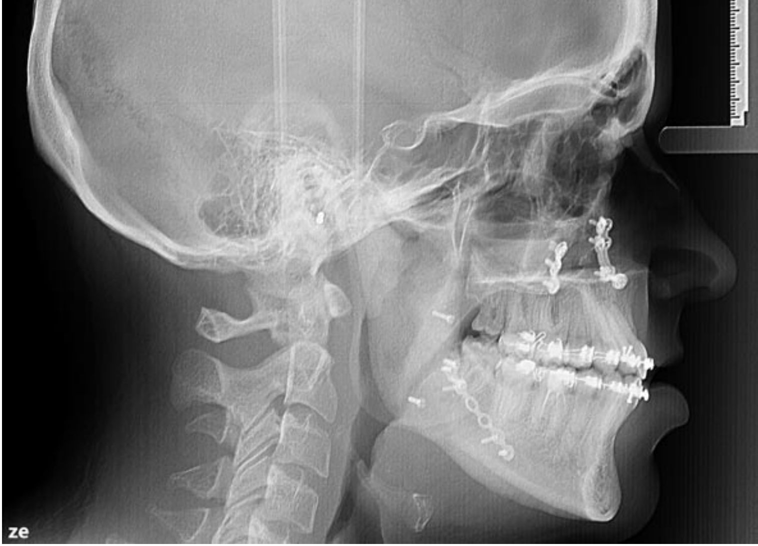


Fig. 12.16a–ze (*continued*) Postoperative images after orthognathic surgery (**zd,ze**; Lefort-I osteotomy and BSSO)

12.5 Primary Chronic Osteomyelitis (at the End): Special Considerations

When putting the Zurich classification together we were fully aware of the fact that there are, and always will be, cases that are extremely difficult to assign. We do understand this classification as a foundation that will change and grow with increasing knowledge. Clearly, there is still much more to understand and research.

Accordingly, at the end of this chapter, we present four cases of primary chronic osteomyelitis of the jaw bone that do not fit into this classical categorization of the Zurich classification as described in this book. The presented cases of this chapter may raise questions thus far not clearly answered and are subject to further discussions. Those cases have been treated and followed in private practice after completion of the 30-year survey at the University in Zurich.

As stated previously, clinical symptoms represent one major characteristic to designate the diagnosis of osteomyelitis; however, especially in primary chronic osteomyelitis, asymptomatic cases may only be recognized by imaging. Since radiological features do not always rule out a neoplastic nature of the lesion, a biopsy specimen is usually required. Frequently these (asymptomatic) cases of primary chronic osteomyelitis are labeled as chronic sclerosing osteomyelitis. We do not understand why these cases develop, since there seems to be no focus, or why the disease remains clinically asymptomatic in these patients. One striking feature seems to be the expansive nature of bone growth, especially in the early stage of young (early-onset) patients. This bony expansion resembles much of fibrous dysplasia. We first present an adult case showing both histological characteristics of primary chronic osteomyelitis and fibrous dysplasia. Furthermore notable is the fact that the patient's grandchild is suffering from primary chronic osteomyelitis of the shoulder underlining a possible genetic nature of disease as suspected in our published case of two sisters (case report 17; Eyrich et al. 2000).

As is typical for primary chronic osteomyelitis, the mandible is also favored by these asymptomatic lesions (case report 20); however, obviously patients may also develop such asymptomatic lesions in other cranial locations such as the zygoma or the maxilla, which is extremely rarely observed in primary chronic osteomyelitis. Since the presented lesions are asymptomatic and do not show other skeletal locations, they do not fall under the term "syndrome-associated primary chronic osteomyelitis" (case reports 18 and 19).

Modern medicine is constantly evolving and developing, we hope, to bring further light to this obscure disease process by sharing and collecting further knowledge and applying new techniques.

12.5 Primary Chronic Osteomyelitis (at the End): Special Considerations

12.5.1 Case Report N° 17

Fibrous Dysplasia and Primary Chronic Osteomyelitis (Clinical Asymptomatic)

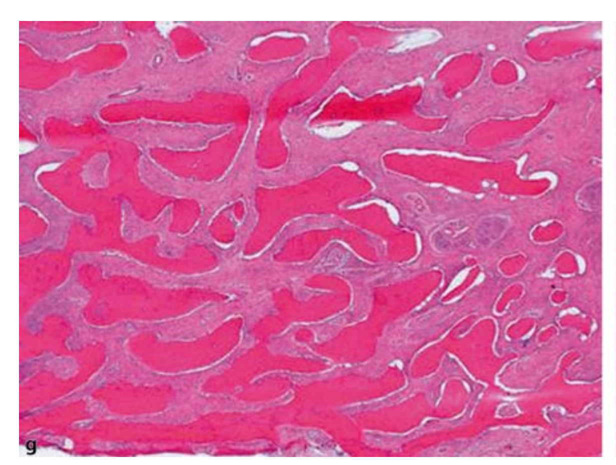
Case Report N° 17 – Summary	
Diagnosis	Old fibrous osseous dysplasia (involving areas of primary chronic osteomyelitis)
Affected bone	Left mandible including joint and ascending ramus
Patient	65-year-old Caucasian woman
General medical history	Arthrosis of the right shoulder The grandchild of the patient suffers from fibrous granulomatous chronic osteomyelitis of the clavicle
Dental/maxillofacial-related medical history	The patient consulted an ENT specialist because of pain in the left ear
Clinical symptoms	Expansive growth in the retromolar region and left ascending ramus
Treatment	Surgical remodeling of bony surplus

A 65-year-old Caucasian woman was referred by her dentist and an ENT specialist for investigation and therapy of an expansive lesion of her left jaw. The patient has not experienced any pain thus far. Initial oral examination revealed a partial edentulous lower jaw with an expansive growth in the retromolar region and the left ascending ramus. The lesion was otherwise inconspicuous (Fig. 12.17a). Initial orthopantomogram showed an expansive growth of the ascending ramus with deformation of the muscular process and increased density of the cancellous bone (Fig. 12.17b). Corresponding CT scans showed sclerotic changes of the bone marrow and loss of cortical bone and bone marrow architecture. A cystic lesion in the lateral aspect of the left condyle was further noted (Fig. 12.17c,d). A bone biopsy harvested from the lesion was labeled as primary chronic sclerosing osteomyelitis by the pathologist (Fig. 12.17g,h). An additional resection specimen of bony surplus remodeling the mandible was first designated as primary chronic osteomyelitis and later the diagnosis was changed by a second pathologist to an old form of fibrous dysplasia. The intraoperative view showed a dense bone pattern (Fig. 12.17e,f). Both biopsies failed to show bacterial growth in microbiological studies.

No further therapy was administered and the patient remains free of symptoms in a 2-year follow-up. No further growth of the lesion has been noted to date.

Acknowledgement: All histology figures of case Report N°16 are courtesy of M. Pfaltz.

Fig. 12.17a–h Oral examination at initial presentation shows the expansive growth of the ascending ramus (**a**). Orthopantomography radiograph at initial presentation (**b**). Note the expansive growth of the ascending ramus with deformation of the muscular process and dense structure of the cancellous bone. Corresponding CT scans at initial presentation (**c,d**). Coronal sections of the ascending ramus show the sclerotic changes of the bone marrow and the loss of cortical bone and bone marrow architecture. A cystic lesion in the lateral aspect of the left condyle is further noted (**c**). Intraoperative site of the ascending ramus (**e**). The dense bone structure can be surmised. Intraoperative site of the ascending ramus shows the osteotomy as part of the surgical remodeling procedure (**f**). **g–h** *see next page*



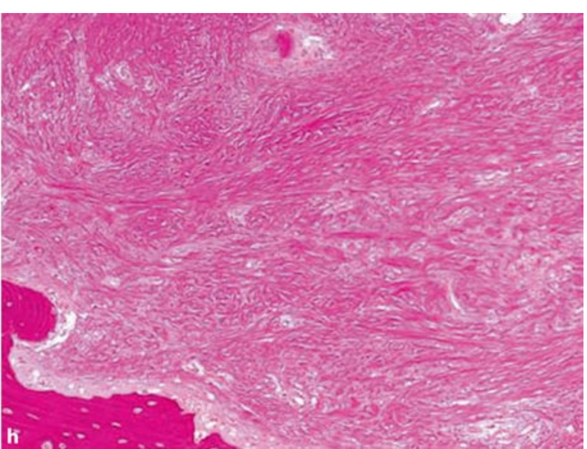


Fig. 12.17a–h (*continued*) Bone biopsies from the resected bone at medium-power magnification (**g,h**; hematoxylin and eosin stain): Sections with typical features of both primary chronic osteomyelitis and fibrous osseous dysplasia are noted (marrow fibrosis, woven bone trabeculae scattered in fibroblastic stroma)

12.5 Primary Chronic Osteomyelitis (at the End): Special Considerations

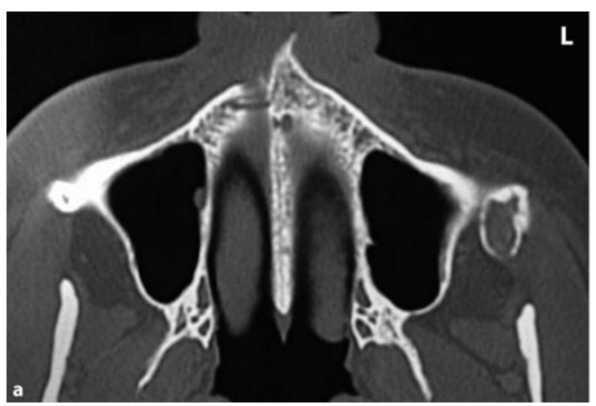
12.5.2 Case Report N° 18

Primary Chronic Osteomyelitis (Clinical Asymptomatic)

Case Report N° 18 – Summary	
Diagnosis	(Primary) Chronic Osteomyelitis (clinical asymptomatic)
Affected bone	Left zygoma
Patient	29-year-old Caucasian woman
General medical history	General, multifocal joint pain
Dental/maxillofacial-related medical history	Silent enhancement in the left zygoma in full-body SPECT investigation
Clinical symptoms	No symptoms in the head and neck region were noted
Treatment	Resection of the bony lesion

A 29-year-old Caucasian patient consulted the primary care physician because of multifocal joint pain involving the ankle, wrist, and back. Laboratory studies showed no signs of rheumatoid disease; however, the steroid medication administered did result in relief of pain. The patient was referred for a SPECT study for further diagnostic work-up, which revealed only enhancement in the left zygoma but no further involvement of joints. The patient was referred for further investigation. The CT scans demonstrated a bony surplus in the left infratemporal fossa anterior to the ascending ramus (Fig. 12.18a,b).Under local anesthesia a biopsy of the lower pole of the lesion was performed. The biopsy specimen was first labeled as a fibro-osseous lesion by the pathologist. Under general anesthesia resection of the affected bone via an enoral route was conducted (Fig. 12.18c,d). The pathologist confirmed necrotic bone, marrow fibrosis, rare signs of inflammation, and signs of bone turnover. The findings were interpreted as a reactive process consistent with findings in primary chronic osteomyelitis; however, a definite designation was not possible (Fig. 12.18e–h). Microbiological studies from the bone specimen showed no growth.

Since the patient showed no symptoms, no further therapy was considered. In a 3-year follow-up the scar showed some tenderness to palpation; otherwise, no complaints or growth was noted.



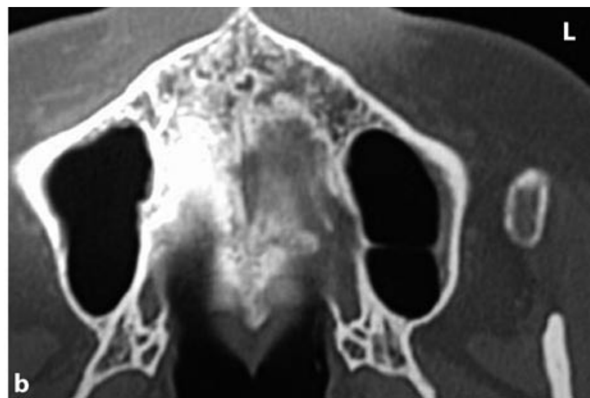


Fig. 12.18a–h Computed tomography scans at initial presentation (**a,b**). Axial sections of the maxillary sinus and zygoma shows the bony surplus in the left infratemporal fossa anterior to the ascending ramus. **c–h** *see next page*

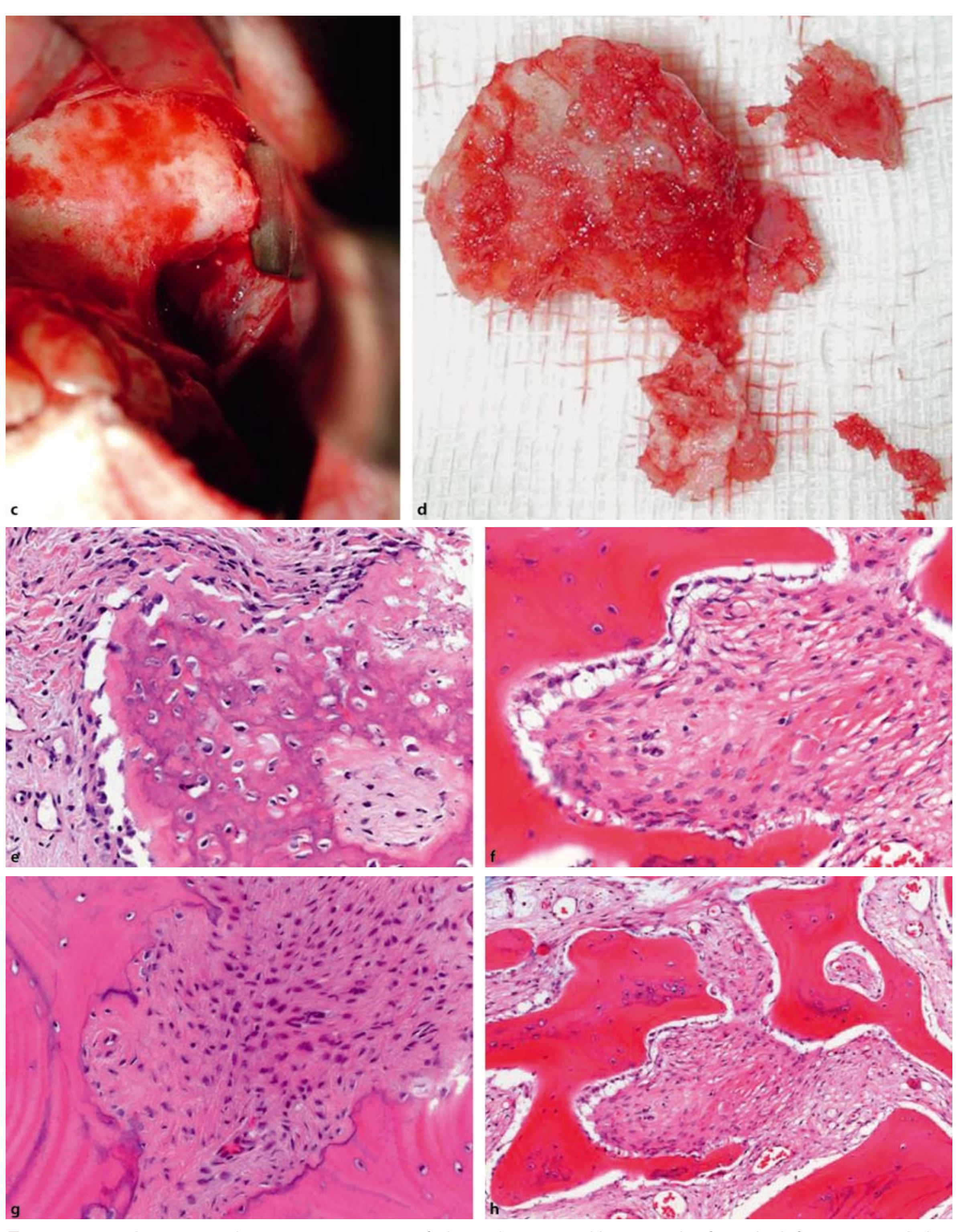


Fig. 12.18a–h (*continued*) Intraoperative site of the zygomatic buttress and the bony tumor (**c**; view from below). Bony specimen from the zygoma (**d**). High-, medium-, and low-power magnification histology sections of the removed bony surplus from the left zygoma (**e**–**h**; hematoxylin and eosin stains). Cortical and cancellous bone with partial bony necrosis, marrow fibrosis, and activity of bony turnover are noted

12.5 Primary Chronic Osteomyelitis (at the End): Special Considerations

12.5.3 Case Report N° 19

Primary Chronic Osteomyelitis (Clinical Asymptomatic)

Case Report N° 19 – Summary	
Diagnosis	Primary chronic (sclerosing) osteomyelitis (clinical asymptomatic)
Affected bone	Left and right maxilla
Patient	15-year-old Caucasian man
General medical history	–
Dental/maxillofacial-related medical history	Early extraction of decayed first maxillary molars (difficult extraction)
Clinical symptoms	No clinical symptoms noted Poor oral hygiene prior to orthodontic therapy
Treatment	Ostectomy of the right-sided lesion

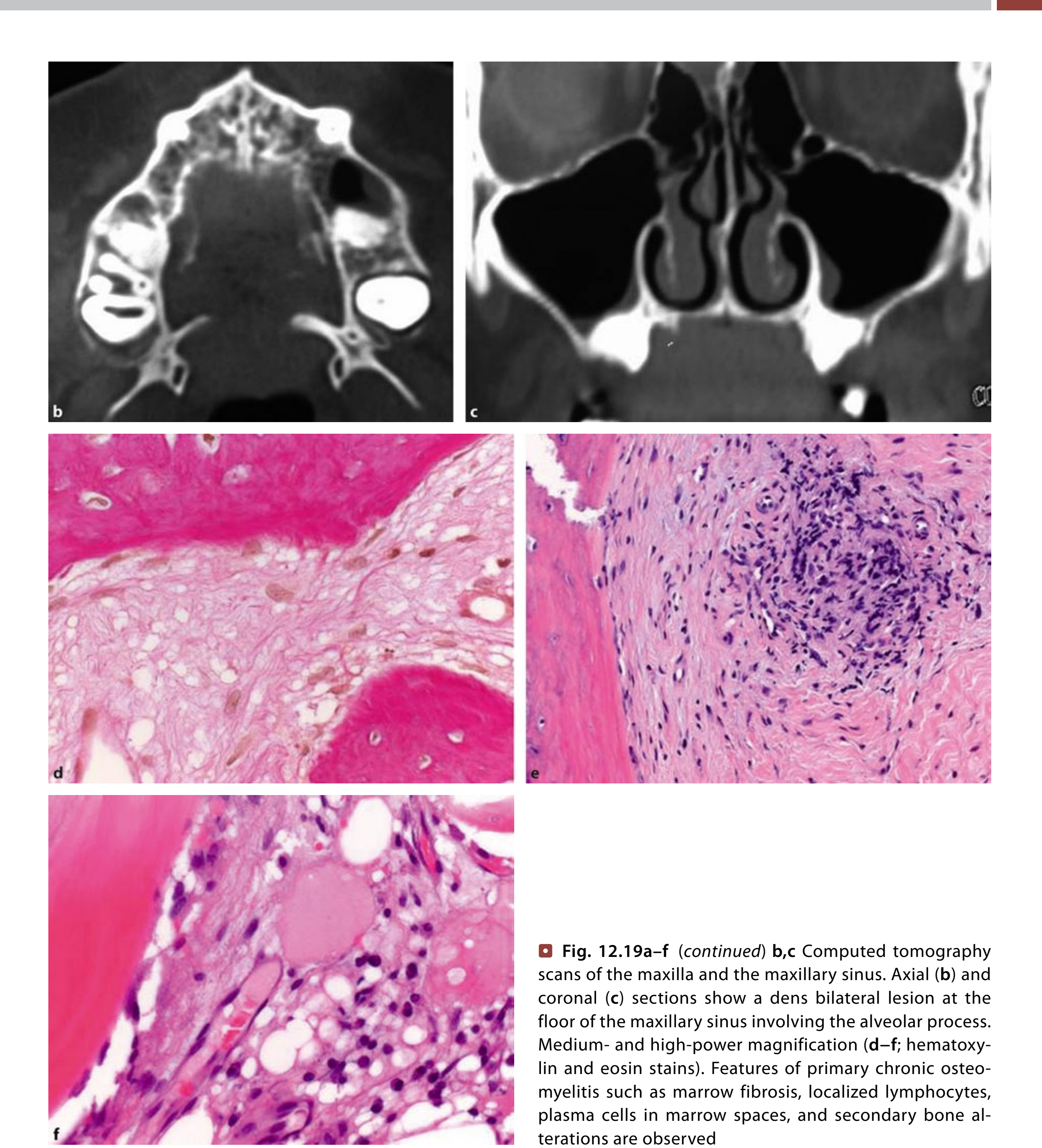
A 15-year-old Caucasian boy was considered for orthodontic treatment. He had a history of early loss of the decayed maxillary molars. The extraction performed by his referring dentist was reported as being difficult. The orthopantomogram prior to orthodontic treatment showed bilateral dense bone and was suspected to be a tumor of odontogenic origin (Fig. 12.19a); thus, the patient was referred to a maxillofacial specialist for further investigation. The CT scans of the maxilla were performed to further evaluate the presumed lesions in the maxilla (Fig. 12.19b,c).

An ostectomy of affected bone on the right side was performed. Pathological work-up of the resected specimen showed findings consistent with primary chronic osteomyelitis (Fig. 12.19d–f). The specimens failed to show any bacterial growth in microbiological studies.

Due to the lack of clinical symptoms, the left side was spared surgery and observed.



Fig. 12.19a–f Orthopantomogram at initial presentation shows bilateral bone densities in the region of the earlier extracted first maxillary molars (**a**). **b–f** *see next page*



■ **Fig. 12.19a–f** (*continued*) **b,c** Computed tomography scans of the maxilla and the maxillary sinus. Axial (**b**) and coronal (**c**) sections show a dens bilateral lesion at the floor of the maxillary sinus involving the alveolar process. Medium- and high-power magnification (**d–f**; hematoxylin and eosin stains). Features of primary chronic osteomyelitis such as marrow fibrosis, localized lymphocytes, plasma cells in marrow spaces, and secondary bone alterations are observed

12.5.4 CASE REPORT N° 20

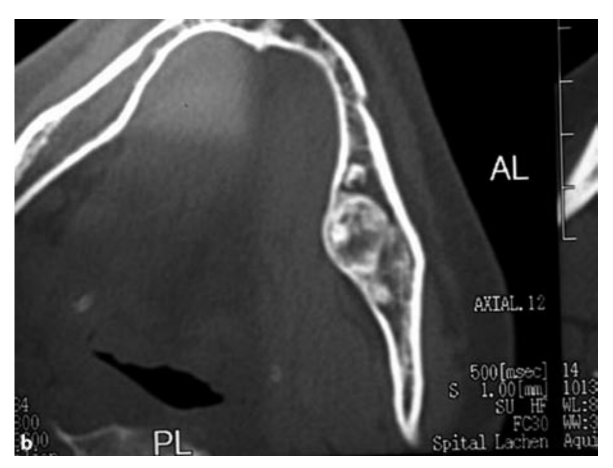
Primary Chronic Osteomyelitis (Clinical Asymptomatic)

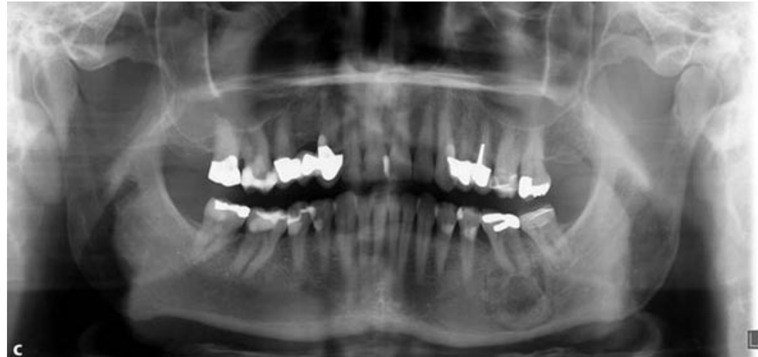
Case Report N° 20 – Summary	
Diagnosis	Primary chronic osteomyelitis
Affected bone	Left mandible first molar region of the mandibular body
Patient	59-year-old Caucasian man
General medical history	Arrhythmia Diverticulosis Recurrent back pain Deviation of the nasal septum
Dental/maxillofacial-related medical history	Asymptomatic concentric mixed pattern lesion of the left mandible
Clinical symptoms	No clinical symptoms were noted prior to surgery
Treatment	Subtotal excision of lesion and filling of the defect with hydroxyapatite graft

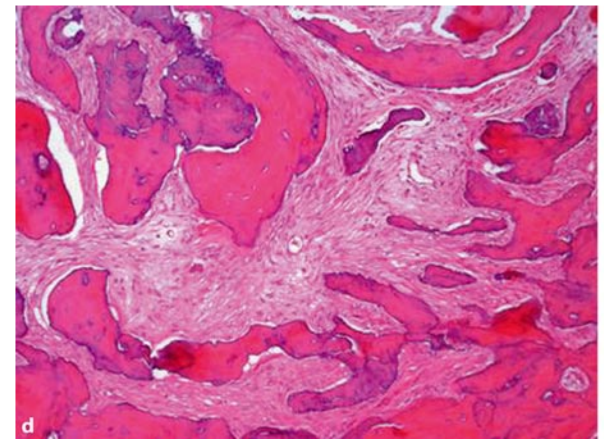
A 59-year-old Caucasian man was referred by his general dentist who discovered a asymptomatic concentric mixed pattern lesion of the left mandible on routine examination (Fig. 12.20a). The tooth 36 was vital on CO2 testing. The patient was referred for further diagnostic work-up and therapy to a maxillofacial specialist. The CT scans performed showed nonhomogeneous lesion expanding the lingual aspect of the mandible (Fig. 12.20b). A biopsy was taken from a lingual approach which showed necrotic bone, signs of inflammation, bone turnover, and hemosiderin deposition. In a further procedure a buccal plate was removed at the site of the lesion, the inferior alveolar nerved freed, and the lesion subtotally removed to harvest more representative material for further histopathological examination. The defect was immediately filled with a hydroxyapatite graft (OsteoBiol®, Tecnoss®, Italy) and the buccal plate was repositioned again (Fig. 12.20c). The harvested specimen now showed clear signs of chronic nonsuppurative bone infection consistent with primary chronic osteomyelitis (Fig. 12.20d,e). Microbiological studies of the resected bone failed to show bacterial growth. No further treatment was administered due to the lack of clinical symptoms. In a 2-year follow-up no complaints or growth was noted.

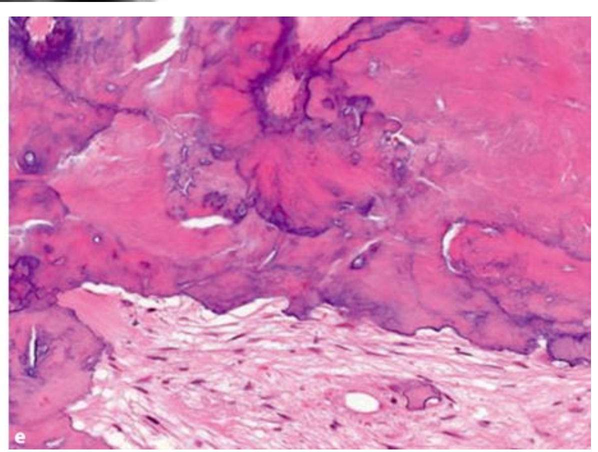


Fig. 12.20a–e Orthopantomogram at initial presentation shows a bony lesion extending from the tip of the roots tooth 36 to the mandibular rim (**a**). **b–e** *see next page*









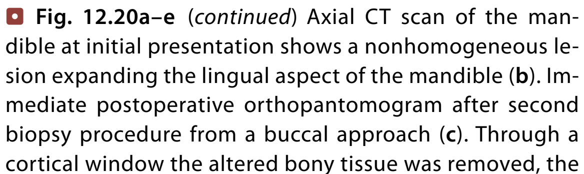


Fig. 12.20a–e (*continued*) Axial CT scan of the mandible at initial presentation shows a nonhomogeneous lesion expanding the lingual aspect of the mandible (**b**). Immediate postoperative orthopantomogram after second biopsy procedure from a buccal approach (**c**). Through a cortical window the altered bony tissue was removed, the medullary space was augmented, and the cortical plate was replaced. Medium-power magnification (**d,e**; hematoxylin and eosin stains) show irregular trabeculae with necrotic bone, loss of osteocytes, dystrophic calcification, fibrotic/fibroblastic cells in marrow spaces, as well as lymphocytes and plasma cells

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Subject Index

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